Malaria outpatient management in government health facilities in Kenya : an evaluation of current practice

Thesis

Malaria outpatient management in government health facilities in Kenya: An evaluation of current practices

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ABSTRACT

Background: Effective case management is a key element of malaria control. Health workers' performance of assessment, diagnosis, treatment and counseling tasks in accordance with evidence-based standards is critical to ensure adequate quality of malaria case management.

Methods: In children below 5 years, the quality of outpatient case management in accordance with national guidelines and factors influencing treatment practices were measured. In older children and adults, the quality of clinical assessment, the accuracy of diagnosis and the ability of clinical signs and symptoms to predict malaria were evaluated. The effects of routine microscopy on malaria case management were described across all-age groups. Data were collected from government facilities in 4 Kenyan districts, in a series of age-specific surveys using a full range of quality of care assessment tools.

Results: The majority (89%) of children with malaria were diagnosed in line with national recommendations; however, only 55% of children with uncomplicated malaria had recommended treatment prescribed. The assessment and counselling components were the weakest parts of the case management. Associations between several programmatic interventions (i.e. training, guidelines, wall charts…) and higher quality of treatment were demonstrated. In older children and adults, the performance of clinical assessment tasks was sub-optimal and massive overdiagnosis (80%) of malaria was apparent. Clinical signs and symptoms showed little promise of being able to improve health worker's ability to predict malaria. While routine microscopy might overcome the

problem it was characterised by inaccuracy (SEN = 67%; SPE = 61%; PPV = 23%; NPV = 92%) and an extremely common practice of ignoring negative results across all age groups (67-78%).

Conclusions: As we embark upon a new era of more expensive and more complex to use antimalarial treatments, improvement in clinical practice and careful consideration of malaria diagnostic strategies are urgently needed. This thesis highlighted the problems, suggests some solutions and provides some support for the view that programmatic approaches might improve health workers performance if implemented effectively at scale.

DEDICATION

To my wife, son and parents,

For their love, dedication, understanding and moral support

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ABBREVIATIONS

ACPR ..... Adequate Clinical and Parasitological Response
ACR ..... Adequate Clinical Response
ACT ..... Artemisinin-based Combination Therapy
AM ..... Antimalarial
AQ ..... Amodiaquine
ARI ..... Acute Respiratory Infections
ART-LUM ..... Artemether-lumefantrine
BS ..... Blood Slide
CAR ..... Central African Republic
CDC ..... Centers for Disease Control
CI ..... Confidence Interval
CBS ..... Central Bureau of Statistics
CDD ..... Control of Diarrhoeal Diseases
CPK ..... Colony and Protectorate of Kenya
CQ ..... Chloroquine
DALY ..... Disability Adjusted Life Year
DH ..... District Hospital
DOMC ..... Division of Malaria Control
DHMT ..... District Health Management Team
EANMAT ..... East African Network for Monitoring of Antimalarial Treatment
EIR ..... Entomological Inoculation Rate
ETF ..... Early Treatment Failure
GDP ..... Gross Domestic Product
GIS ..... Geographic Information System
GoK ..... Government of Kenya
GPS ..... Global Positioning System
HC ..... Health Centre
HF ..... Health Facility
HW ..... Health Worker
HMIS ..... Health Management Information Systems
HRP-II ..... Histidine Rich Protein II
IEC ..... Information Education Communication
IM ..... Intramuscular
IMCI ..... Integrated Management of Childhood Illness
ITN ..... Insecticide Treated Nets
IV ..... Intravenous
KEMRI ..... Kenya Medical Research Institute
KES ..... Kenyan Shilling
KNMS ..... Kenya National Malaria Strategy
LPF ..... Late Parasitological Failure
LTF ..... Late Treatment Failure
MoH ..... Ministry of Health
MSH ..... Management Sciences for Health

NCPD ..... National Council for Population and Development
NGO ..... Non-governmental Organisation
NMCP ..... National Malaria Control Programme
NPV ..... Negative Predictive Value
OPD ..... Outpatient Department
OR ..... Odds Ratio
pLDH ..... Parasite Lactate Dehydrogenease
PCR ..... Polymerase Chain Reaction
PPV ..... Positive Predictive Value
PR ..... Prevalence Rate
QN ..... Quinine
RBC ..... Red Blood Cells
RDT ..... Rapid Diagnostic Test
RBM ..... Roll Back Malaria
SEN ..... Sensitivity
SPE ..... Specificity
SP ..... Sulfadoxine-pyrimethamine
SPR ..... Slide Positivity Rate
UNICEF ..... United Nations Children's Fund
USD ..... United States Dollars
µl ..... microlitre
WBC ..... White Blood Cells
WHO ..... World Health Organisation

CHAPTER 1:

Introduction and literature review

1.1 Malaria – the biology of transmission

1.1.1 Malaria parasites

The discovery in 1880 by Charles Louis Alphonse Laveran of the causative organism of malaria in a patient with intermittent fever in Algeria was one of the milestones in the history of medicine (Wernsdorfer & McGregor, 1988). Malaria is a parasitic disease caused by a unicellular protozoan of the genus Plasmodium, family Plasmodiidae, suborder Haemosporidiidae, order Coccidia. There are about 120 species of Plasmodium found in the blood of mammals, reptiles and birds. Four commonly infect humans: *Plasmodium falciparum, P. vivax, P. ovale* and *P. malariae. P. falciparum* is the commonest species throughout the tropics and subtropics, most prevalent in sub-Saharan Africa and is responsible for the greatest part of malaria's global morbidity and mortality. *P. vivax* has the widest geographical range; it is prevalent in many temperate zones, as well as in the subtropics and tropics. *P. malariae* is focally distributed over the same range as *P. falciparum* but much less common. *P. ovale* occurs mainly in sub-Saharan Africa, but also in the West Pacific (Lysenko & Beljaev, 1969).

1.1.2 Malaria vectors

Mosquitoes of the genus *Anopheles* were first identified as the vector of malaria in 1897 in India when Sir Ronald Ross discovered pigmented parasite's oöcysts on the stomach wall of an *Anopheles* mosquito (Wernsdorfer & McGregor, 1988). The subfamily Anophelinae belongs to the family Culicidae of the order Diptera and comprises 3 genera: *Chagisa*, *Bironella* and *Anopheles*. *Anopheles* is the only genus known which is able to transmit human malaria. Of around 430 known species of *Anopheles* mosquitoes,

70 are malaria vectors and only 40 are of medical importance (Service & Townson, 2002). Though most common in tropical and subtropical regions, *Anopheles* mosquitoes have an almost worldwide distribution with different mix of species transmitting malaria in various parts of the world.

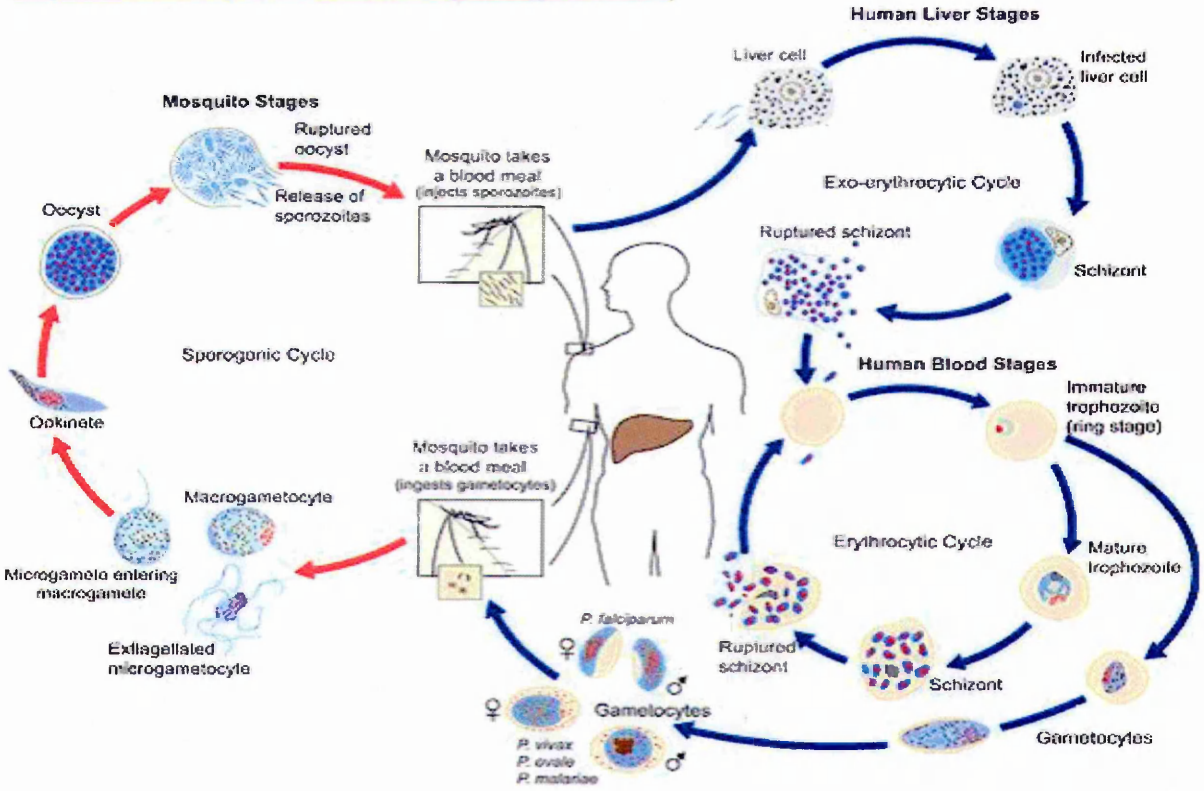
A group of species with common morphological criteria and line of descent comprise a species complex, whose constituent members may differ in their host preference, breeding sites, favoured sites for resting or feeding and even their capacity to transmit malaria. The *An. gambiae* complex is the dominant malaria vector in Africa. It is comprised of seven species: *Anopheles gambiae sensu stricto (s.s.)*, *An. arabiensis*, *An. melas*, *An. merus, An. quadriannulatus*, *An. quadriannulatus* Species B and *An. Bwambae* (Coluzzi, 1984). The most medically important in the complex are two: 1) *An. gambiae s.s,* a fresh water breeder, predominant in humid areas, preferring feeding on humans and resting indoors, and a highly efficient malaria vector, and 2) *An. arabiensis,* a fresh water breeder which bites humans and may rest indoor, but it often feeds on cattle and rests outdoors, and is more tolerant of the drier savannah regions. *An. gambiae s.s.* and *An. arabiensis* are found in 70% of the African continent and *An. funestus* is the next most abundant vector in tropical Africa (Gillies & Coetzee, 1987; Lindsay *et al.*, 1998).

1.1.3 Life cycle of the malaria parasite

A fundamental discovery in the history of malaria occurred in 1898 when Sir Ronald Ross and Giovanni Batista Grassi described the complete transmission cycle of *Plasmodium* in birds and humans respectively (Wernsdorfer & McGregor, 1988). All

malaria parasites develop in two phases and require the presence of two hosts to complete their life cycle: the exogenous sexual cycle (*sporogony*) develops in their definitive host, *Anopheles* mosquito, and the endogenous asexual cycle (*schizogony*) in the human, their intermediate host (Figure 1.1). The asexual cycle consists of two phases that take place in the blood (*erythrocytic schizogo*ny) and in the liver (*exo-erythrocytic schizogony*).

Figure 1.1: Life cycle of *Plasmodium* in man and in the mosquito
(http://www.cdc.gov/malaria/biology/life_cycle.htm)



1.1.3.1 Sexual cycle of the parasite in the mosquito host

The female Anophelene needs a human blood meal to support production of eggs. After ingesting blood, the asexual stages of the parasite are digested together with the red blood cells in the stomach of the mosquito while the mature sexual cells (gametocytes) continue

further development. After completion of the maturation process of the female gametocytes and exflagellation process of the male gametocytes, the fertilisation between male and female gamete occurs, resulting with the creation of a zygote.

Within 18-24 hours the zygote develops into an oökinete which forces its way through the mosquito's stomach wall, settles down on its outer surface and is now called an oöcyst. Within each oöcyst an average of 1000 sporozoites are produced which burst the wall of the cyst and enter the mosquito's body cavity. Sporozoites find their way to the salivary glands of the female *Anopheles* which now becomes infective and awaits the mosquito's feeding on a vertebrate host. The duration of the sporogony is affected by the ambient temperature and can take between 7 days if the environmental temperature is about 31°C, to 20 days if the temperatures are about 20°C (Wernsdorfer & McGregor, 1988).

1.1.3.2 Asexual cycle of the parasite in the human host

After the mosquito bites a human host, the sporozoites pass with saliva into the peripheral circulation in which they circulate for a short time, usually less than 60 minutes. Many of them are destroyed by phagocytes but some invade parenchymal liver cells (hepatocytes) where they develop and multiply in a process known as *exo-erythrocytic schizogony* or *the tissue phase.* Here, sporozoites develop into schizonts that produce large numbers of merozoites per hepatocyte (10,000–30,000 depending on the parasite species) and release them into the circulation. The liver Kupffer cells ingest much of the released merozoites, but some escape and reach the peripheral circulation to invade erythrocytes. They reach

erythocytes within a few minutes and the invasion takes only about 30 seconds. The duration of the *tissue phase* can be as short as 5.5 days for *P. falciparum* and as long as 16 days for *P. malariae*. *P. vivax* and *P. ovale* are able to form a dormant liver stage, the hypnozoite, that release merozoites into the peripheral circulation at a later point in time and cause relapsing malaria.

The youngest stages of the parasite within the erythrocytes have an annular appearance and are known as *ring forms*. As they grow they become more irregular in shape. All early stages of the parasite within the erythrocytes are called trophozoites. They digest haemoglobin and leave a pigment called haemozoin that can be seen by microscopy in the body of the parasite. Trophozoites multiply asexually to form schizonts within which up to thirty merozoites develop and these are released into the blood circulation. Merozoites invade young erythocytes, multiply within them and cause their rupture. Peaks of fever are coincidental with the ruptures of erythrocytes as a response to the release of toxins into the blood circulation. The erythrocytes rupture in synchronised 48-hour cycles in *P. falciparum*, *P. vivax* and *P. ovale* infections and in 72 hours cycles for *P. malariae*. A small fraction of merozoites will develop at later rounds of erythrocyte invasion into the sexual forms of parasites, the gametocytes, which are taken up by mosquitoes during the blood meal to continue the cycle.

1.1.4 Measures of transmission

The underlying principles of malaria transmission dynamics are common to many infectious diseases and can be summarised as the probability that a susceptible host

becomes infected on contact with a pathogen. A variety of mathematical models of the probability of transmission have been developed, most have used as their basis those developed by Ross and Macdonald (MacDonald, 1957). The most common descriptions of the probability of malaria transmission are the basic reproduction rate and the vectorial capacity. The basic reproduction rate is defined as the average number of new cases of disease that will arise from the introduction of an infective host into a wholly susceptible population. Specifically for malaria, the basic reproduction rate is defined as the average number of successful offspring that a parasite can potentially produce (MacDonald, 1957). The vectorial capacity is defined as the mean number of probable inoculations transmitted from one case of malaria in a unit of time (Anderson & May, 1992). Intensity of malaria transmission may vary within short geographical distances and over time within and between years, the size of variations mainly determined by the time and space variations of malaria seasons, local climate and susceptive ecologies for malaria transmission.

1.1.5 Describing malaria endemicity

The term endemicity refers to the intensity of malaria transmission and has been used since the 1950s to indicate the amount or severity of malaria in an area. Malaria is generally described as endemic when it is normally found in a population, as opposed to non-endemic when transmission is non-existent or very sporadic, either in areas that never had malaria or in areas where endemic malaria has been eradicated by successful anti-malarial interventions. Conventionally, if malaria disease ceased to be transmitted over at least 3 years in area malaria is no longer endemic.

Endemic malaria transmission may be broadly classified as stable or unstable depending on the amount of variation present in malaria transmission over time. Under stable endemic conditions, there is a temporal continuation of year-to-year transmission, however variation in the amount of malaria may exist within and between years. On the other hand, unstable malaria is characterised by great and irregular variability in transmission over space and time. Malaria epidemics may be considered a form of highly unstable malaria.

1.1.5.1 Measures of the endemicity

The entomological inoculation rate (EIR) is the most direct measure used to describe the intensity of malaria transmission across endemic areas. EIR is defined as the number of infective mosquito bites received per person per unit of time, usually, expressed per year. The annualised EIR is the preferred measure of malaria endemicity as it reflects the incidence of new infections received by the human population exposed to the local vectors. The values of EIR from the various malaria endemic areas of Africa may range from one infective bite every 3 years up to several infective bites every night (Hay *et al.*, 2000). However, given the complexity of data collection, non-standardized methods of measurement (Githeko *et al.*, 1996), frequent difficulties in the interpretation of the results (Mbogo *et al.*, 2003) and most importantly the overall paucity of reliable data (Hay *et al.* 2000), the EIR is rarely used as a marker for mapping malaria endemicity in sub-Saharan Africa (Rogers *et al.*, 2002).

Other methods, more commonly used to measure malaria endemicity, are the prevalence of peripheral blood-stage infections (*parasite rate*) and the proportion of enlarged spleens (*spleen rate*) in the childhood population. The classification of malaria endemicity based on parasite and spleen rates was introduced at WHO conference in Kampala in 1950 and later revised in relation to the parasite rate only (Metselar & Van Thiel, 1959). The descriptive classification of malaria endemicities and their definitions based on the parasite and spleen rates have not changed over the years and are presented in Table 1.1.

Table 1.1: Descriptive classification of malaria endemicity based on parasite and spleen rates

Type	Spleen rates	Parasite rates
Hypoendemicity	Not exceeding 10% in children 2-9 years	Not exceeding 10% in children 2-9 years but may be higher for part of the year
Mesoendemicity	Between 11% and 50% in children 2-9 years	Between 11% and 50% in children 2-9 years
Hyperendemicity	Constantly >50% in children 2-9 years. Also high in adults (>25%).	Constantly over 50% among children 2-9 years.
Holoendemicity	Constantly >75% in children 2-9 years. But low in adults.	Constantly over 75% among infants 0-11 months.

1.1.5.2 Global distribution of malaria endemicity and population

Recently, Hay *et al.* (2004) and Snow *et al.* (2005) have reviewed the past, present and future of the global distribution of malaria in relation to the population and endemicity classes. They have shown that malaria has been markedly reduced in its spatial distribution during the 20th century and that the global surface of malarious areas was decreased by nearly half; from 77.6 million km^2 in 140 countries occupying 53.2% of global land surface during the pre-control period in 1900, to 39.8 million km^2 in 88 countries occupying 27.2% of land surface in 2002. However, global population growth from 1 to 6 billion during the 20th century has resulted in a 2 billion increase in the total population exposed to malaria risk. During the 20th century, human efforts to control

malaria have been most successful at lower endemicity ranges with reductions of the epidemic, hypoendemic, and mesoendemic areas of 100%, 66% and 45%, respectively. Conversely, there were negligible effects in areas of hyperendemic and holoendemic malaria with reductions of only 16% and 0%, respectively.

Today, the global distribution of malaria endemicity indicates that 19.6% of malarious areas are hypoendemic, 32.2% are mesoendemic, 31.2% are hyperendemic and 12.6% are holoendemic. The majority of the global population at risk live in hypoendemic areas (51.2%) followed by mesoendemic (30.0%) and combined hyper-holoendemic areas (18.8%). The population living in Africa accounts for only 23.6% of the global population at malaria risk, however, within hyper-holoendemic class nearly all (99.7%) population at risk is situated on this continent. The distribution of population across malaria endemicity is markedly different in Africa compared to other regions. While in Africa only 7.5% of the population lives in hypoendemic areas, the same endemicity class accounts for 50.1% of population at risk in other parts of the world. Snow *et al.* (2005) estimates of the populations at malaria risk in 2002 across WHO world regions and malaria endemicity are presented Table 1.2.

Table 1.2: Populations (millions) at risk in 2002 by WHO region and malaria endemicity (Snow *et al.*, 2005)

	Population according *P. falciparum* endemicity classes				
	Unclass-ified	**Hypo - endemic**	**Meso-endemic**	**Hyper-holo endemic**	**Total population at risk**
Africa	13.6	39.3	67.4	414.3	521.0
Americas	3.5	43.9	10.5	0	54.5
South East Asia	47.8	827.6	486.0	0.3	1,313.9
Western Pacific	22.4	77.6	63.4	1.0	142.0
Eastern Mediterranean	32.3	143.0	33.4	0	176.4
Europe	1.1	0.3	3.2	0	3.5
World	120.7	1,131.7	663.9	415.6	2,211.3

1.2 Burden of malaria

In an effort to define disease-specific mortality rates and aid cross-country comparisons, the Disability Adjusted Life Year (DALY) is a widely accepted measure. DALYs are the sum of life years lost due to premature mortality and years lived with disability adjusted for severity. In 2001, it was estimated that malaria was the eighth largest contributor to the overall burden of disease globally, the eighth highest contributor to the global DALY and the second in Africa (WHO, 2002a).

1.2.1 Malaria morbidity burden

The global burden of malaria is thought to be between 300 and 500 million clinical cases each year, with about 90% of these occurring in sub-Saharan Africa, mostly caused by *P. falciparum* (WHO, 2000a). However, more recent estimates by Snow *et al.* (2005) revealed that there were 515 (range: 300-660) million episodes of clinical *P. falciparum* malaria in 2002, of which 365 million (71%) were in Africa. These estimates are significantly higher than those reported previously, reflecting the WHO's reliance upon passive national reporting in countries outside Africa. With regard to the endemicity class, the majority (68.5%) of malaria cases worldwide occur in combined hyper-holoendemic areas, of which nearly all (99.7%) are in Africa. Snow *et al.* (2005) estimates of the burden of *P. falciparum* clinical attacks in 2002 across WHO world regions and malaria endemicity are presented Table 1.3.

Table 1.3: *P. falciparum* malaria cases in 2002 (millions) by WHO region and endemicity (Snow *et al.*, 2005)

	P. falciparum endemicity classes			Total
	Hypo-endemic	Meso-endemic	Hyper + Holo-endemic	
Africa	1.69	11.52	351.77	364.98
Americas	1.89	1.80	0	3.69
South East Asia	35.59	83.11	0.24	118.94
Western Pacific	3.34	10.84	0.85	15.03
Eastern Mediterranean	6.15	5.71	0	11.86
Europe	0.01	0.54	0	0.55
World	48.67	113.52	352.86	515.05

1.2.2 Malaria mortality burden

Worldwide, between 1.1 and 2.7 million people die of malaria each year, of whom about 1 million are children under the age of 5 years in sub-Saharan Africa (WHO, 2000a). The estimates of mortality burden in sub-Saharan Africa have varied between 0.5 and 2 million malaria deaths each year (Bruce-Chwatt, 1952; Sturchler, 1989; Greenwood, 1990; Schwartlander, 1997); however, a lot of skepticism has been raised about the methodological validity of these approximations. The estimates provided by Snow *et al.* (2003a) employed empirical epidemiological measures of mortality risks, structured according to age and malaria transmission. It is similar to the approach used previously by Snow *et al.* (1999), which estimated 1 million malaria deaths in sub-Saharan Africa, but is cognisant of new data, refined endemicity classifications, broader health consequences and temporal effects associated with changing anti-malarial drug sensitivity.

Therefore, the most recent estimates suggested that 1.14 million malaria deaths occurred in 2000 in sub-Saharan Africa, of which 64.8% were in children below 5 years of age, 18.8% in older children 5-14 years and 16.3% in adults above 14 years of age (Snow *et al.*, 2003a).

1.2.3 Indirect burden of malaria infection

There are a number of features of the malaria related burden that are not a result of direct and immediate clinical effects of malaria infection but are consequential to malaria disease. Patients who survive severe malaria may be left with debilitating sequelae, such as neurological or cognitive impairments (Mung'Ala-Odera *et al.*, 2004). In sub-Saharan Africa, Snow *et al.* (2003a) estimated that the number of children impaired each year following cerebral malaria is between 2,700 and 3,000 for epilepsy; 7,000 to 7,800 for learning difficulties; and 770 to 860 remain with severe deficits including quadriparesis. Furthermore, the management of severe malaria anaemia with blood transfusion might contribute a further 5,300 to 8,500 HIV related deaths in endemic Africa each year. Likewise, the adverse drug reactions, such as hepatotoxicity, agranulocytosis and aplastic anaemia, consequent upon managing febrile illness could further contribute a minimum of 2,500 deaths.

1.2.4 Burden of malaria in pregnancy

The relation between adverse effects of malaria infection in pregnancy and premature births, low birth weight and maternal anaemia is well recognised (Murphy & Breman, 2001). In a review provided by Guyatt & Snow (2001), the median prevalence of severe

anaemia among pregnant women across sub-Saharan Africa was reported to be 8.2%, of which 26% are assumed to be due to malaria. The authors estimated that 400,000 pregnant women may have developed severe anaemia as a result of malaria infection in 1995. Brabin *et al.* (2001) suggested that malaria-associated anaemia contributes to 3.7% of maternal mortality in sub-Saharan Africa or approximately 5,300 maternal deaths annually. Furthermore, it has been estimated that between 71,000 and 190,000 children will die during the first year of life because they were born of low-birth weight as an indirect result of their mother's being infected by *P. falciparum* in 2000 (Snow *et al.*, 2003a).

1.2.5 Burden of fevers

Patient's history of fever is the entry point for presumptive diagnosis and treatment practices for malaria across Africa, and underpins the basis of case management guidelines (Gove, 1997; WHO, 2000a; 2003a). It should be recognised that not all reports of fever are febrile and not all febrile episodes are malaria. However, when examining demand for services and commodities such as antimalarial drugs the incidence of perceived fever is more important than the precise incidence of clinical malaria. With this caveat in mind it is obvious that the estimates of the burden of fevers would be several-fold higher than estimates of malaria burden. In 2000, in sub-Saharan Africa, Snow *et al.* (2003b) estimated that the age-structured annual burden of fevers was 850 million in children below 5 years of age, 640 million among children aged 5–14 years and 1,350 million among adults. Currently, when expensive, artemisinin-based combination therapies (ACT) are promoted as treatments for malaria, the burden of malaria fevers is

of critical importance to estimate appropriate volume of drugs and funds required to support an effective policy transition.

1.2.6 Economic burden of malaria

To show the effect of malaria on the economic welfare of affected countries, Gallup and Sachs (2001) performed a cross-country regression analysis, taking into account initial poverty, economic policy, life expectancy, climatic, geographic, and colonial history specificities, among other factors. The authors showed that a 10% decrease in malaria was associated with a 0.3% increase in the Gross Domestic Product (GDP) per capita annually, while countries with intensive malaria had 1.3% lower growth in GDP per capita. They also reported that countries that had eliminated malaria experienced increased economic growth, while the countries with intensive malaria had income levels in 1995 of only 33% that of countries without malaria. Malaria and poverty are thus closely connected, however the high levels of malaria in poor countries are not mainly a consequence of poverty, but are more determined by climate and ecology.

1.3 Malaria – description and epidemiology of disease

Malaria is an acute febrile disease with extremely diverse clinical manifestations. The severity and course of disease will depend on the species and strain of infecting parasite; as well as the age, genetic constitution, state of immunity, general health and nutritional status of the patient, and the effects of any chemoprophylaxis or chemotherapy that has been used. Although the clinical presentations of malaria differ between species and

patients, the best-known presentation of malaria, commonly used as the hallmark of the disease, is the febrile paroxysm, or "ague attack" as it was described historically.

1.3.1 Classical febrile paroxysm

The classical pattern of the febrile paroxysm has been summarised by Wernsdorfer and McGregor (1988) as having three stages. First, there is a cold stage when the patient feels extremely cold, clutches at blanket, may shiver and his teeth frequently chatter. The skin is usually cold and dry, commonly with goose pimples and cyanotic blueness. The cold stage lasts for some 15 minutes to an hour, the temperature gradually rises and the shivering eventually ceases. The second stage is the hot stage when the patient feels intense heat. The skin is hot and dry, the face is flushed, and the respiratory rate is increased. The pulse is full and bounding, and the blood pressure tends to fall. Patients may complain of headache, parched throat, thirst, vomiting, restlessness and excitability. The progression towards delirium is possible. The temperature may reach 40°C or higher and usually remains at about the level reached by the end of the "cold" phase, however, sometimes it may rise further and even reach hyperpyrexial levels. Young children may develop convulsions. The hot stage usually lasts for two hours or more, finishes with peripheral vasodilatation and continues into the third, or sweating, stage. This stage is characterised with profuse perspiration and the feeling of relief since the symptoms of the previous stage disappear. The temperature then falls and may become within normal limits. The patient feels exhausted and usually falls asleep. When he or she wakes up the patient may feel well and prepared to continue his/her daily routine. The entire three-

stage paroxysm lasts some 6-10 hours, and may occur at any time of the day, but usually in the late afternoon and in the evening.

The paroxysm coincides with the rupture of mature erythocytic schizonts. The period between paroxysms is termed the interval. The interval is determined by the length of the asexual cycle. *P. falciparum, P. vivax and P. ovale* have 48 hours cycle and the paroxysms occur on alternate days (or following *tertian* pattern on days 1 and 3 according to the ancient Roman way of counting). *P. malariae* has a 72 hours cycle causing *quartan* paroxysms on days 1 and 4. However, the periodicity of febrile paroxysms will develop only if the patient is left untreated and the infection is highly synchronized, so that the erythrocytes containing mature schizonts rupture at the same time. Furthermore, even at synchronized infections, intermittent fever is usually absent at the beginning of the disease when other non-specific symptoms are predominant.

1.3.2 Clinical presentation of *P. falciparum* malaria in non-immune patients

The most detailed accounts of the clinical presentation of malaria in non-immune patients have been described in the 1920's when neurosyphilis was treated with induced malaria parasites (James, 1931; Shute, 1951; Chernin, 1984). Initially, any species of malaria was used for malaria therapy but it soon became apparent that *P. falciparum* did not adhere to the history of the disease followed by other *Plasmodium* species, and caused much more severe disease requiring more patient care (Shute, 1951).

Several days or hours before the first febrile attack, one or a combination of non-specific prodromal symptoms may occur. They can include headache, dizziness, malaise, pains in the neck, back, limbs or joints, mild gastrointestinal symptoms (nausea, anorexia, diarrhoea and vomiting) and transient fever not exceeding 37.7°C. The classical febrile paroxysm followed by an afebrile asymptomatic interval, based on the *tertian* periodicity of the asexual cycle, is unusual. *P. falciparum* paroxysms tended to be longer, with irregular fevers, better described as continuous or remittent. Rarely, the intermittent fevers would still have occurred, and if they did, the febrile paroxysms could follow daily (*quotidian)*, every third day (*tertian*) or twice every three days (*subtertian*) pattern.

A variety of symptoms ranging from mild headache to severe prostration accompanied fever in the patients with induced malaria. It was observed that the greater severity was not necessarily associated with a higher parasite load, asynchronous infections lead to a more severe symptomatology than synchronized ones and the intermittent fevers with long intervals were associated with more pernicious signs than fevers with short intervals.

1.3.3 Clinical presentation of *P. falciparum* malaria in patients living in endemic areas

Functional immunity acquired by prior infections may modify the classical clinical presentation of malaria described previously in non-immune patients. Several observational studies have described clinical features associated with *P. falciparum* malaria across a range of malaria endemicities in Africa. Schmitz & Gelfand (1976) provided a clinical account from Zimbabwe. They reported age-specific frequencies of clinical features among malaria parasitaemic patients, the majority of them (95%) due to

P. falciparum. Most patients above 7 years of age had fever (93%), headache (73%) and splenomegaly (52%). Less common clinical features included vomiting (39%), abdominal pains (38%), cough (26%), chest pain (21%), hepatomegaly (19%), diarrhoea (17%), general pains (16%), back pain (15%), constipation (14%), leg pain (14%), joint pain (13%) and dysuria (12%), among others. In children below 7 years, fever was the most common feature (70%), followed by splenomegaly (64%) and hepatomegaly (51%). Less commonly, cough (29%), diarrhoea (22%), abdominal pains (15%) and vomiting (13%) among the others, were present.

Among adult patients in Tanzania, Mkawagile & Kihamia (1986) reported that headache (95%), fever (90%), myo-arthralgia (90%), and nausea and vomiting (15%) were the most common symptoms. Basset *et al.* (1991) described an all age group sample of clinically diagnosed malaria patients without parasitological confirmation in Zimbabwe. They reported that the most common clinical features were headache (85%), feeling hot (73%), body weakness (73%), chills (65%), joint pains (56%) and abdominal pains (51%). In Kenya, Freeman (1986) provided a detailed account of the clinical presentation among malaria parasitaemic patients across four age groups and two areas of different malaria endemicity (Table 1.4).

Table 1.4: Frequency of malaria signs and symptoms across age groups and two areas of endemicities, Nyanza Province, Kenya (Freeman, 1986)

	Mesoendemic				Holoendemic			
Age (yrs)	½ - 1 ½ (%)	1 ½ - 4 (%)	5 – 14 (%)	15 – 90 (%)	½ - 1 ½ (%)	1 ½ - 4 (%)	5 – 14 (%)	15 – 90 (%)
Fever	100	100	100	81.8	100	93.3	66.7	100
Headache	-	-	-	95.7	-	-	-	100
Chills	55.9	64.0	88.0	86.9	0	13.3	20	0
Splenomegaly	48.6	57.7	41.7	8.7	70.0	80.0	70.0	0
Anorexia	62.9	57.7	56.0	47.8	30.0	53.3	53.3	50.0
Vomiting	37.1	42.3	40.0	13.0	40.0	6.7	33.3	25.0
Diarrhoea	38.2	46.2	8.0	30.4	40.0	33.3	46.7	25.0
Drowsiness	35.3	34.6	47.8	56.5	0	7.0	6.5	12.5
General malaise	64.5	55.9	78.3	82.6	0	13.3	7.0	50.0
Abdominal pain	-	-	-	55.2	-	-	-	50.0
Joint pain	-	-	-	78.3	-	-	-	37.5
Convulsions	8.8	26.9	8.3	0	0	6.7	0	0

The majority of malaria patients living in endemic areas develop an uncomplicated malarial attack and recover either spontaneously without medical intervention or by taking antimalarial drugs. However, a small proportion, particularly of non-immune children, will progress towards severe disease and may eventually die. The clinical presentations of severe forms of *P. falciparum* malaria are described in the following section.

1.3.4 Severe forms and complications of *P. falciparum* malaria

Severe *P. falciparum* malaria is defined by the presence of potentially fatal manifestations or complications of malaria in patients with asexual forms of *P. falciparum* for whom other diagnoses have been excluded (WHO, 1986). The other functional definition of severe malaria is malaria requiring inpatient care. WHO has specified clinical and laboratory criteria for severe and complicated malaria and they include the following: coma, severe malarial anaemia, hypoglycaemia, circulatory

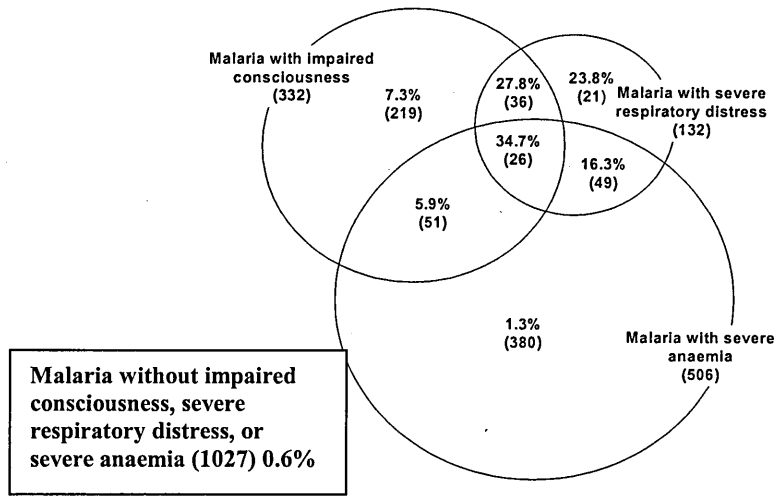
collapse, renal failure, pulmonary oedema, spontaneous bleeding, repeated convulsions, acidosis, haemoglobinuria, impaired consciousness, jaundice, prostration, hyperpyrexia and hyperparasitaemia (described in Warrell *et al.*, 1990). Most of the recommended WHO criteria, however, were not based on observations made in African children, the population accounting for 90% of *P. falciparum* associated mortality.

Marsh *et al.* (1995) provided the first comprehensive clinical description of severe malaria in African children. The authors studied 1,844 children admitted to a paediatric ward in a Kenyan hospital with a primary diagnosis of malaria and calculated the frequency and mortality rate for each of the clinical and laboratory criteria comprising WHO defined severe malaria. The results indicated that the prevalence of WHO criteria among children with severe malaria were the following: coma (10.0%), severe malarial anaemia (17.6%), hypoglycaemia (13.2%), respiratory distress as substitute for WHO criterion of pulmonary oedema (13.7%), circulatory collapse (0.4%), renal failure (0.1%), spontaneous bleeding (0.1%), repeated convulsions (18.3%), haemoglobinuria (0.1%), impaired consciousness (8.2%), jaundice (4.7%), prostration (12.2%), hyperpyrexia (10.6%) and hyperparasitaemia (8.9%).

Furthermore, Marsh *et al.* (1995) demonstrated that children presenting with clinical and laboratory features not including impaired consciousness, severe respiratory distress or severe anaemia were associated with very low mortality (0.6%). A striking conclusion from this study was that life-threatening malarial disease in African children, as defined by poor outcome in the presence of good management, was mostly present within two

overlapping syndromes: malaria with impaired consciousness and malaria with severe respiratory distress. The mortality rate in children with severe malarial anaemia was 4.7%, but in the majority, who had neither impaired consciousness nor severe respiratory distress, it was only 1.3% (Figure 1.2).

Figure 1.2: Prevalence, overlap and mortality for major clinical sub-groups of severe malaria in children – total numbers are in parenthesis and mortality is given as percentage (Marsh *et al.*, 1995)



1.3.5 Epidemiology of malaria disease

One of the most important factors affecting the epidemiology of malaria disease is the acquisition of functional immunity caused by the repeated infections during a lifetime. At present there are no valid immunological markers to directly relate immune responses to the various risks of clinical malaria, however, certain epidemiological features of immunity have been examined through the relation between age and various exposure patterns of malaria disease.

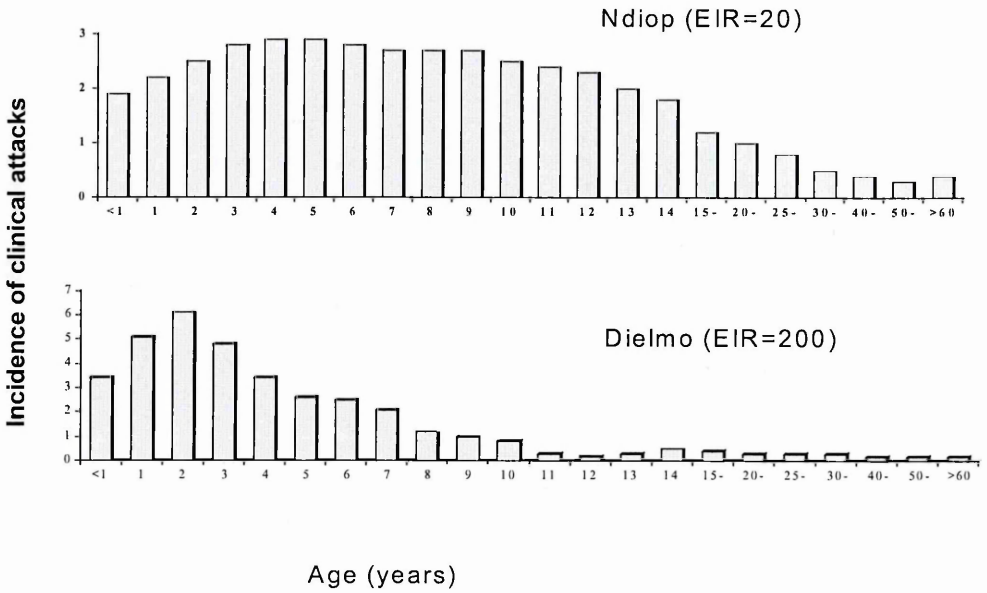
1.3.5.1 Pattern of mild malaria by age and transmission intensity

The relation between the age, intensity of transmission and mild malaria morbidity during childhood has been summarised by Snow & Marsh (1998). The authors analysed age-specific (1-7 years of age) incidence of mild malaria from six areas of different transmission intensities in Tanzania, Ghana, Senegal, Sierra Leone and The Gambia. The results illustrated two major features: 1) among the populations exposed to high intensity of transmission, rates of mild morbidity declined throughout a childhood, whilst the incidence of mild malaria in lower transmission settings showed minor age-specific variations in the same period; and 2) under all transmission settings, with the exception of the holoendemic area, the incidence of malaria was lower in the first year of life compared to the second year of life.

Few studies have examined the incidence of mild malaria across all age groups. In Senegal, Trape & Rogier (1996) compared the age-specific incidence of mild malaria between two markedly different transmission settings. In a high transmission setting (EIR = 200) the incidence of clinical attacks peaked in early childhood (age of 2 years) and rapidly declined afterwards. However, in an area of moderate transmission (EIR = 20), the peak incidence came later (age of 5 years), remained constant during late childhood and declined in teenage years and adulthood (Figure 1.3). It might be expected that populations living in high transmission settings would have a higher overall incidence of malaria than populations living in low transmission areas. Interestingly, despite these marked differences, Trape & Rogier (1996) reported from Senegal that the overall number of clinical episodes was approximately equal in both areas, and if anything higher

in low transmission setting. However, these analyses did not examine the clinical severity of such episodes and this is the subject of discussion in the following section.

Figure 1.3: Clinical malaria attacks in two areas of differing transmission intensity in Senegal (Trape & Rogier, 1996)



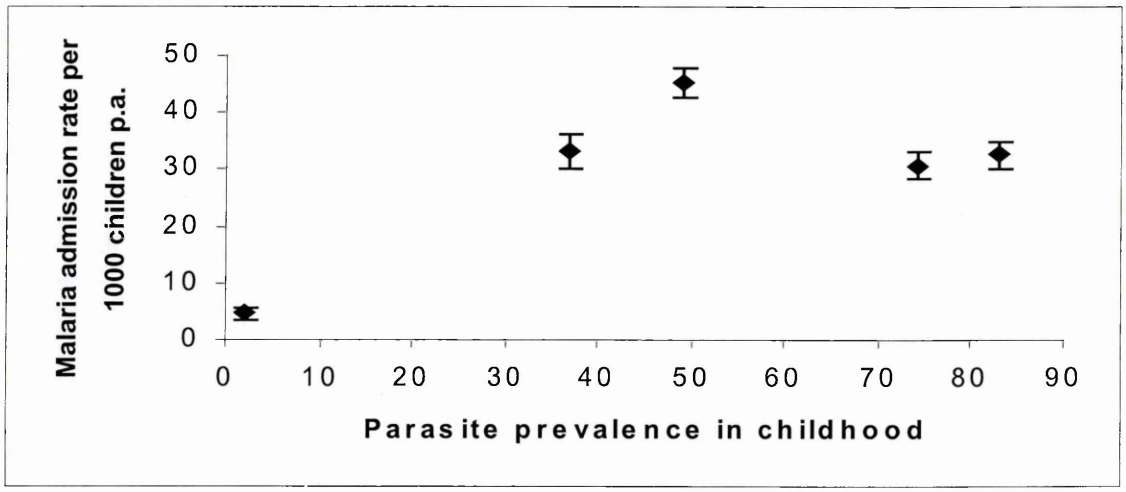
1.3.5.2 Pattern of severe malaria by age and transmission intensity

Snow *et al.* (1997) presented the age-specific pattern of severe malaria admissions from five sites of different malaria transmission intensities in Kenya and The Gambia. The childhood prevalence of *P. falciparum* infection at these sites ranged from the lowest, 2% in Bakau, The Gambia to the highest, 83% in Siaya, Kenya. The prevalence at the remaining sites was 37% at Sukuta, The Gambia, 49%, Kilifi North, Kenya and 74% at Kilifi South, Kenya. The mean age of paediatric malaria admissions below 10 years of age increased from 17 months at two sites of the most intense transmission to 63 months at the lowest intensity transmission site.

At two sites with most intense transmission, the risks of developing severe disease were the highest during the first two years of life; thereafter the risks declined rapidly and from the age of 3 years remained at a low level of less than 10 episodes/1,000 children/year. In areas of moderate transmission, the risks of severe disease peak at the age of one year and then declines gradually to a level of about 10-25 episodes/1,000 children/year in the 5 year olds. In the area of lowest malaria transmission, the disease risk was evenly spread throughout childhood at low rates of less than 10 episodes/1,000 children/year.

Consistent with observations of mild disease in Senegal (Trape & Rogier, 1996), an overall rate of severe malaria admissions in children 0-9 years old was lower in areas of high transmission intensity than in areas of moderate transmission (Figure 1.4). This pattern was markedly pronounced for cerebral malaria, notable for low incidence in areas of high malaria transmission (Snow *et al.*, 1994). The findings of these studies were in accordance with the study in Brazzaville, Congo where the incidence of severe malaria was approximately the same across different settings, indeed the lowest in children exposed to the most intense transmission (Trape *et al.*, 1987). Here, the critical issue to arise is whether the patterns described for mild and severe disease would remain true for deaths from malaria in the community. This issue is discussed in the next section.

Figure 1.4: Incidence of severe malaria admissions per 1000 children aged 1-59 months per year from five communities with different malaria transmission intensities (Snow *et al.*, 1997)



1.3.5.3 Malaria mortality and transmission intensity

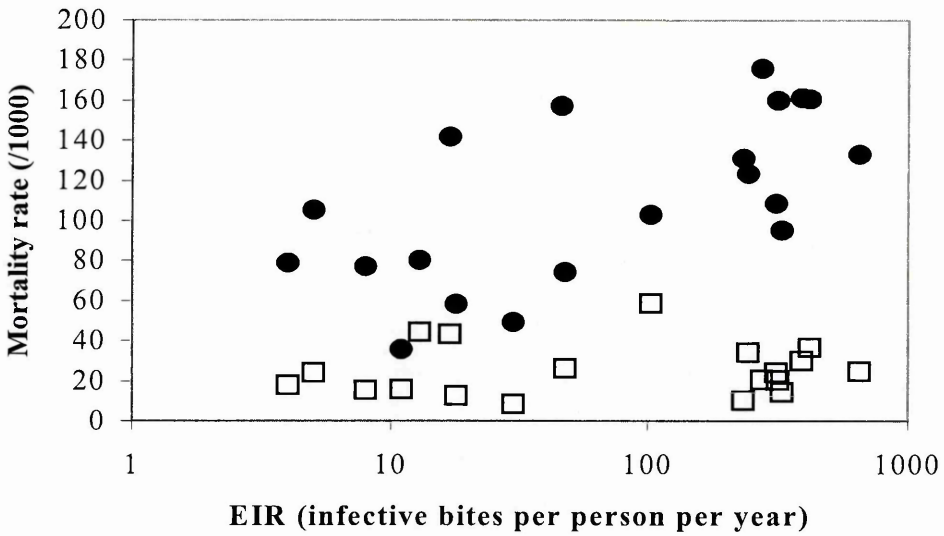
Intuitively, it might be expected that the majority of malaria deaths would occur in areas with the highest malaria transmission. However, in a review of 11 studies on malaria specific mortality at different levels of transmission, Snow & Marsh (1995) showed that, in spite of various limitations of the data, a number of interpretations of malaria mortality were possible with regard to the increase of malaria transmission: malaria mortality could rise, reach a plateau or fall with increasing transmission.

These observations created considerable debate and a series of analyses of the same and additional data followed (Trape & Rogier, 1996; Lengeler *et al.*, 1997; D'Alessandro & Coosemans, 1997; Shiff, 1997; Trape, 1997; Greenwood, 1997). Interpretations of these comparative studies can be broadly divided into those which concluded that malaria mortality amongst children aged less than 5 years rises linearly with increasing

transmission intensities and those which showed that initial linear rises in mortality saturate under conditions of moderate-to-high transmission.

A more recent addition to this debate was provided by Smith *et al.*, (2001) who reviewed published and unpublished data from 1980-1999 and looked at all-cause mortality in infants 0-11 months and children 1-5 years of age against an estimate of the intensity of transmission as measured by the EIR. The data showed that all-cause mortality in infants increased with transmission intensity, however, there was no difference in the mortality rate in the children 1-5 years of age with increasing transmission (Figure 1.5).

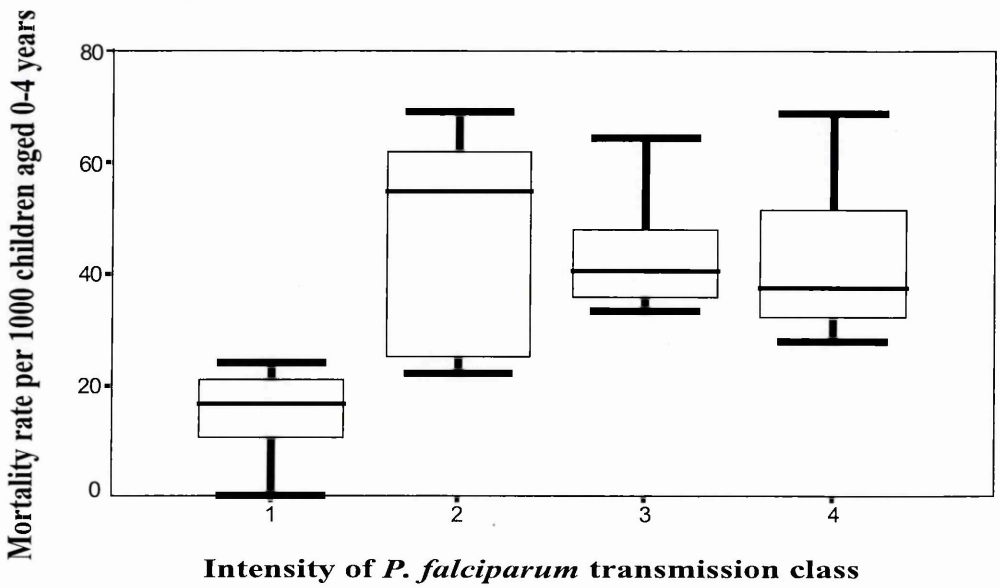
Figure 1.5: Distribution of all-cause mortality 0-11 months (closed circles) and 12-59 months (squares) from 20 sites in Africa by the annual *P. falciparum* entomological inoculation rate (Smith *et al.*, 2001)



A further recent and comprehensive contribution to this debate was a review provided by Snow & Marsh (2002) on 26 studies conducted since 1980 where all-cause mortality from 0-5 years was measured, but instead of EIR, the mortality data points were categorised according to whether the parasite prevalence rates was less than 25% (low

transmission intensity), 25-50% (low-to-moderate transmission intensity), 51-74% (moderate-to-high transmission intensity) and greater than 74% (high transmission intensity). The authors concluded that children living under low intensity of transmission have all-cause mortality rates about half of those of children living under moderate-to-high transmission. The second striking observation, consistent with the analysis provided by Smith *et al.* (2001), was that deaths in the first year of life rise linearly with increasing exposure to malaria over a wide range of transmission intensities. By contrast all cause mortality under 5 years appears to vary very little within a broad range of malaria transmission intensities and saturates at relatively low levels of transmission (Figure 1.6).

Figure 1.6: Box plot showing median (central lines), 25%, 75% quartile ranges around the median (box width) and upper and lower limits (T) all-cause childhood mortality per 1000 children aged 0-4 years per annum recorded during the surveillance of communities located in (1) areas of low, (2) low-to-moderate, (3) moderate-to-high or (4) high intensity transmission (Snow & Marsh, 2002)



The public health importance of these findings with regard to the interventions that reduce exposure to malaria parasites, such as insecticide treated nets (ITNs), has been

summarised by Snow & Marsh (2002). The authors concluded that ITNs would have the greatest impact when used in areas where burden of malaria is high but the frequency of parasite exposure is low-to-moderate. In areas of high transmission, initial reductions in mortality may prove difficult to sustain as the reduced level of transmission may still lie on the part of the curve where mortality has saturated.

1.3.5.4 Summary of the age impact on malaria infection, morbidity and mortality

In most areas of malaria transmission the age-specific curves of parasite prevalence, mild and severe disease, and malaria deaths shift right with increasing intensity of transmission if all other factors were held constant. Parasite prevalence peaks in an older age group in areas of moderate transmission and much earlier for those in areas of high transmission. The rate of mild malaria begins to fall in older ages compared to declines in risk of severe malaria. The rates of severe malaria drop very rapidly and there are few cases of severe malaria and malaria deaths in older children and adults.

1.4 Malaria diagnosis

Traditionally in clinical practice, a case of malaria is confirmed upon microscopic demonstration of *Plasmodium* parasites in a patient presenting with the clinical features of the disease, the most important hallmark being fever. However, in most African settings, especially at the periphery of the health care system, microscopic support to diagnose malaria is not available and malaria is routinely diagnosed on a clinical basis only. In this section the accuracy of current practices in diagnosis of malaria are

summarised, clinical and laboratory approaches to diagnosis of malaria are reviewed and the public health importance of malaria diagnosis is discussed.

1.4.1 Accuracy of clinical malaria diagnosis in Africa – current practices

A striking feature of the clinical presentation of malaria in the semi-immune patient is the large variety of signs and symptoms that can mimic many other acute febrile illnesses, such as pneumonia (Redd *et al.*, 1992; O'Dempsey *et al.*, 1993; Källander *et al.*, 2004), bacteraemia (Akpede *et al.*, 1992; Berkley *et al.*, 1999), typhoid (Richens *et al.*, 1992) and bronchitis (Williams, 1940). Given the non-specific presentation of malarial signs and symptoms and frequent recommendations suggesting treatment of all fevers as malaria (Gove, 1997; WHO, 2000a; 2003a), current health worker practices result in significant overdiagnosis of malaria cases. The high rate of overdiagnosis has been reported from numerous studies across different age groups across various intensities of malaria transmission.

In several studies focusing on childhood populations across Africa (Nigeria, Tanzania, Kenya and Senegal), 37-80% of the patients diagnosed clinically as malaria did not have a positive malaria smear (Hendrickse *et al.*, 1971; Okeahialam *et al.*, 1972; Freeman, 1986; Gaye *et al.*, 1989; Nsimba *et al.*, 2002). Similarly, the studies looking at adult patients in Tanzania and Malawi reported 52-76% of malaria overdiagnosis (Mkawagile & Kihamia, 1986; Jonkman *et al.*, 1995, Font *et al.*, 2001). In several studies including patients across all age groups, the overdiagnosis rates were reported to range between 56-77% (Stein & Gelfand, 1985; Basset *et al.*, 1991; Font *et al.*, 2001; Barnish, 2002).

Two studies reported the differences in health workers diagnostic accuracy between different malaria transmission seasons. In Niger, the rate of overdiagnosis during the high and low transmission season was 46% and 96% respectively (Olivar *et al.*, 1991). Similar results were reported from Namibia: 51% of patients were overdiagnosed during wet season and 93% during dry season (Barnish, 2002). In Kenya, Freeman (1986) compared diagnostic accuracy between two areas of different malaria endemicities and reported higher rates of overdiagnosing among all age group patients in holoendemic (67%) compared to mesoendemic areas (48%). On the other hand, in children below 15 years of age, the frequency of overdiagnosis was equal (37%) between both areas of malaria endemicity.

1.4.2 Clinical algorithms for the diagnosis of malaria

As described in the previous section, the problem and magnitude of malaria overdiagnosis has been recognised for some time. In response to this problem, several research groups have attempted to improve malaria diagnostic accuracy based on signs and symptoms alone. Extensive exploration of clinical algorithms has been done primarily in children; however, a few studies have investigated clinical predictors of malaria among older children and adults. Chandramohan *et al.* (2002) have provided a comprehensive review of the studies investigating clinical algorithms in children. The performance of various algorithms suggested by the reviewed studies is presented in Table 1.5.

In most of the clinical predictors studies in children, a malaria case was defined as a child with a fever or a history of fever in the presence of malaria parasitaemia. Several studies used fever and a cut-off parasitaemia of 5,000 parasites/µl as a gold standard malaria diagnosis (Weber *et al.*, 1997; Olaleye *et al.*, 1998; Bojang *et al.*, 2000). The significant association between individual clinical predictors and gold standard malaria diagnosis (measured as relative risk or odds ratios) was demonstrated for a variety of signs and symptoms. However, all signs and symptoms associated with malaria in the univariate logistic regression analysis, demonstrated poor sensitivities and specificities on their own. The sensitivity and specificity of the clustered groups of the clinical predictors or the clinical scores generated, usually improved the accuracy (Table 1.5.); however, no malaria case definition or clinical score with the improved specificity had an acceptable level of sensitivity to justify withdrawal of an antimalarial treatment in a febrile child (Marsh *et al.*, 1996; Chandramohan *et al.*, 2002).

A further complication of the proposed clinical algorithms in children is that their performance is usually site and time specific, depending on the intensity of malaria transmission and prevalence of other diseases in the community. The most illustrative example comes from The Gambia where two studies undertaken in areas of similar malaria endemicity and following the same methodology failed to suggest the same clinical predictors (Olaleye *et al.*, 1998; Bojang *et al.*, 2000). The predictive values of the clinical algorithm improved during the malaria season in Niger (Rougemont *et al.*, 1991); but also with the increase of the acute lower respiratory infections in the Philippines (Gomes *et al.*, 1994). However, in one study in Ethiopia, it was suggested that the

algorithms performed better during the low malaria season (Muhe *et al.*, 1999). The poor predictive values revealed in the study undertaken in low endemic area in India, prompted authors to conclude that the algorithms perform even more poorly in malaria low endemic than in high endemic areas (Chandramohan *et al.*, 2001).

Table 1.5: Clinical algorithms derived for the diagnosis of non-severe malaria in children (Chandramohan *et al.*, 2002)

Country	SPR (%)	Species (%)	Criteria with the best predictive values	Sen (%)	Spe (%)	PPV (%)	NPV (%)
Tanzania[1]	59	Pf 97 Pm 3	Intermittent fever 2-3 days	73	98	99	71
Philippines[2]	67[a]	Pf 67 Pv 22 Mixed 11	History of fever + (chills and/or sweating)	55[a]	79[a]	84[a]	46[a]
	37[b]			50[b]	89[b]	77[b]	70[b]
Papua New Guinea[3]	73	Pf 55 Pv 22 Pm 6	Enlarged spleen + no cough	NR	NR	90	NR
			Temperature ≥38°C[c]	NR	NR	46[c]	NR
Rural Malawi[4]	60	Mostly Pf	Rectal temperature ≥37.7°C or nailbed pallor or splenomegaly	85	41	68	64
Gambia[5]	7	Mostly Pf	Chills, sweating or shaking	93 94[d]	19 19[d]	8 5[d]	97 99[d]
Thailand[6]	24	Pf 43 Pv 50 Mixed 7	History of fever +headache + no cough	51	72	64	59
Ethiopia[7]	30[e]	Pf 58 Pv 42 Mixed 1	History of fever+ headache + no cough	83[e]	51[e]	42[e]	87[e]
	6[f]			75[f]	60[f]	11[f]	97[f]
Gambia[8]	39	Mostly Pf	Weighted Malaria Score ≥8[i]	88[g]	64[g]	65[g]	87[g]
			Weighted Malaria Score ≥9[i]	61[g]	82[g]	72[g]	73[g]
Gambia[9]	35	Mostly Pf	Weighted Malaria Score ≥7[i]	89[h]	63[h]	56[h]	90[h]
			Weighted Malaria Score ≥8[i]	70[h]	78[h]	63[h]	82[h]
India[10]	7	Pf 16 Pv 83 Mixed 1	Unweighted Malaria Score ≥3[j]	80	37	10	95
			Unweighted Malaria Score ≥4[j]	60	61	11	94

[a] Among children enrolled at home; [b] Among children enrolled at the study clinic;
[c] Predictive values refer to diagnosing malaria with parasite density ≥10,000/µl;
[d] Predictive values refer to diagnosing malaria with parasite density ≥5000/µl;
[e] Parasite prevalence and predictive values refer to high transmission season;
[f] Parasite prevalence and predictive values refer to low transmission season;
[g] Predictive values refer to malaria with temperature ≥38°C plus parasite density ≥5000/µl;
[h] Predictive values refer to malaria with temperature ≥37.5°C and parasitaemia ≥5000/µl;
[i] Weighted Malaria Score was calculated from the following nine predictors: Sleepy, reduced feeding, absence of cough, shivering, feels hot, cough not heard, pallor of palm, absence of rash, increased respiratory rate. Each predictor was given a score of 1 if present and 0 if absent except feeling hot which was given 3 if present and 0 if absent.
[j] Unweighted Malaria Score was calculated from the following 10 predictors: chills, feeling cold, vomiting absence of cough, absence of runny nose, absence of diarrhoea, feels hot, palpable spleen, palpable liver, axillary temperature ≥3.7°C. Each predictor was given a score of 1 if present and 0 if absent.
[1] Rooth & Bjorkman (1992); [2] Gomes *et al.* (1994); [3] Genton *et al.* (1994); [4] Redd *et al.* (1996); [5] Weber *et al.* (1997); [6] Luxemburger *et al.* (1998); [7] Muhe *et al.* (1999); [8] Olaleye *et al.* (1998); [9] Bojang *et al.* (2000); [10] Chandramohan *et al.* (2001).
SPR = slide positivity rate (≥1 parasite of any species); **Sen** = sensitivity; **Spe** = specificity; **PPV** = positive predictive value; **NPV** = negative predictive value; **Pf** = *P. falciparum*; **Pv** = *P. vivax*; **Pm** = *P. malariae*; **NR** = not reported

Only four studies have investigated clinical predictors in adult patients while only one focused on older children. In patients above 15 years of age in a low endemic area of

India, Chandramohan *et al.* (2001) proposed a model including the following predictors: chills, feeling cold after an episode of fever, feeling hot to touch, temperature > 37 °C, vomiting, palpable spleen, palpable liver, absence of cough, absence of diarrhoea and absence of runny nose. The best performing clinical score of 5 demonstrated poor sensitivity (55%) and specificity (58%).

In the same age group in a holoendemic area of Papua New Guinea, Genton *et al.* (1994) reported that the absence of cough and normal stools were the only predictors associated with a positive blood slide, while only vomiting was associated with parasitaemia >10,000 parasites/μl. In a holoendemic area in Tanzania, Oster *et al.* (2000) observed among adult patients that some of the clinical criteria such as difficulties in breathing, sore throat, chest pain and cough, abnormal chest sounds and enlarged lymph nodes were associated with a diagnosis other than malaria, however the sensitivities of predictors presented were generally unsatisfactory (range: 17-55%).

In an area of moderate malaria transmission in Kenya, Mwangi *et al.* (2005) suggested 9 clinical predictors in older children (5-14 years) and only 3 predictors in adults (>14 years). The predictors associated with malaria diagnosis in older children were: temperature ≥37.5°C, shivering, vomiting, normal chest sound, absence of rhinitis, cough not heard, absence of wounds, absence of rashes and palpable spleen. Three predictors associated with malaria in adults were: patient hot on palpation, joint pains and absence of chest pain. Individually, all predictors in both age groups had either poor sensitivities or poor specificities when cross-tabulated with malaria diagnosis. In older children the

best performing score of 5 had a sensitivity of 86% and a specificity of 72%, performing better than the best performing score of 2 in adults (sensitivity of 29% and specificity of 84%).

The conclusion of most studies that have explored clinical algorithms across all age groups and different areas of malaria endemicity is that the validity of malaria diagnosis based on signs and symptoms is largely unsatisfactory and that laboratory confirmation is required to improve diagnostic accuracy.

1.4.3 Laboratory methods for diagnosis of malaria

The major laboratory methods for diagnostic confirmation of malaria include light microscopy, fluorescence microscopy, detection of specific nucleic-acid sequences and rapid diagnostic tests (RDT). The light microscopy and RDTs are the methods that have potential for widespread routine use in Africa and are described in the following sections.

1.4.3.1 Light microscopy

Conventional light microscopy, using blood obtained from a finger prick and examining both, the thick and thin blood smear is an established method for the laboratory confirmation of malaria. Giemsa staining is recommended as the standard method, Field's stain is an option (Lema *et al.*, 1999), and both methods are superior to Wright's stain (Haditsch, 2004). The thick blood smear concentrates the layers of red blood cells and improves the detection of low parasitaemias compared to the thin blood smear; however, the thin blood smear is preferred method for the routine differentiation of

parasite species (Moody, 2002). By examining the thick blood smear, the experienced microscopist can detect as low as 5-10 parasites per µl, however, under routine field conditions the detection of 100 parasites per µl is a more realistic target (WHO, 2000b).

To estimate the parasite density, a parasite count per 1 µl of blood using the standard value of 8000 white blood cells (WBC) is a recognised method (Moody, 2002). Counting the number of parasites present until 200 WBC have been seen and then multiplying the number of parasites by 40 will give the parasite count per µl. Another method includes counting the number of parasites in 100 fields and multiplying by four to give parasites per one µl, assuming a blood volume of 0.25 µl per 100 microscopic fields (Kilian *et al.*, 2000). A simpler plus system method for enumerating parasites and indicating the relative parasite count should be used only when it is not possible to undertake a parasite count per µl of blood (WHO, 1991). The plus system results should be reported as 1-4 codes according to the following definitions:

\+ = 1-10 parasites per 100 thick-film fields

++ = 11-100 parasites per 100 thick-film fields

+++ = 1-10 parasites per thick-film field

++++ = more than 10 parasites per thick-film field

The parasitaemia may also be estimated in the thin blood smear by calculating the number of parasitised red blood cells (RBC) seen in 10,000 RBCs and expressing the number of parasitised cells seen as a percentage (Moody, 2002). While microscopic

examination is accepted as the current gold standard method for the diagnosis of malaria, there is no accepted single standard method for the quantification of parasites. If the comparisons between parasitaemias are to be made it is of paramount importance that exactly the same methods are applied for their quantification.

Although microscopy is a sensitive, informative and inexpensive method, and recognised as a gold standard method for malaria diagnosis, it is also labour-intensive and time-consuming, depending absolutely on good techniques, reagents, microscopes and, most importantly, well trained and supervised technicians (WHO, 2000b).

1.4.3.2 Rapid diagnostic tests

Malaria rapid diagnostic tests (RDT) are lateral flow immunochromatographic tests, which are based on the capture of parasite antigen from peripheral blood using monoclonal antibodies prepared against a malaria antigen target. Malaria antigens currently targeted by RDTs are: 1) histidine-rich protein II (HRP-II) produced by trophozoites and young gametocytes of *P. falciparum* (Shiff *et al.*, 1993); 2) parasite lactate dehydrogenease (pLDH), an enzyme produced by all blood stage parasites (Piper *et al.*, 1999); and 3) *Plasmodium* aldolase, an enzyme produced by all four species (Moody, 2002).

The first malaria RDT marketed was ParaSight F test, an HRP-II-based assay capable of detecting *P. falciparum* (Shiff *et al.*, 1993). Today, at least 25 branded products are commercially available, the majority targeting *P. falciparum* alone (WHO, 2003b). Some

RDTs are capable of distinguishing between *P. falciparum* and non-*P. falciparum* species, however, they do not differentiate non-*P. falciparum* species from each other, and mixed infections of *P. falciparum* and non-*P. falciparum* species from *P. falciparum* monoinfections. The persistence of HRP-II antigenaemia after malaria therapy has limited the use of this antigen for the clinical monitoring of the therapeutic response (Humar *et al.*, 1997; Wongsrichanalai, 2001); however, pLDH-based assays representing only viable parasites have overcome this problem and its detection was closely related to the microscopic demonstration of the parasites (Moody, 2002). Semi-quantitative correlation between the RDT band intensity and level of parasitaemia has been observed for both HRP-II and pLDH tests; however, the variability was considerable (Forney *et al.*, 2001; Craig *et al.*, 2002; Mason *et al.*, 2002).

The early studies evaluating the accuracy of RDTs showed promising results (Beadle *et al.*, 1994; Garcia *et al.*, 1996; Palmer *et al.*, 1998; Quintana *et al.*, 1998). The systematic reviews of the earlier studies generally agreed that RDTs are capable of detecting *P. falciparum* with sensitivities >90% and with specificitity close to 100% at parasitaemias higher than 100 parasites/μl of blood (Hänscheid, 1999; Wongsrichanalai, 2001; Moody, 2002).

In more recent studies, however, the variability of the RDT performance characteristics significantly increased, both within and between RDTs. Murray *et al.* (2003) reviewed the studies undertaken after 2000 and reported that the sensitivity for detection of *P. falciparum* ranged from 35-97% with specificities of 77-100%; for *P. vivax* or non-*P.*

falciparum species the variability in the sensitivities was even greater (range: 2-97%) while specificity ranged from 97-100%. It has been thought that the recent poor results may reflect increased exposure of RDTs to the environment during the transport and storage, poor quality of RDTs perhaps as result of scaling up to larger manufacturing lots, but also the fact that researchers may now be more willing to publish poor results (WHO, 2003b).

Although, the accuracy of RDTs is the most important parameter and further refinements in this aspect are required by the industry, there are several advantages of RDTs over traditional microscopy. RDTs do not require electricity, special equipment or complex health worker training. Several studies have shown that volunteer health workers can be successfully trained to perform tests correctly (Bell *et al.*, 2001; Cho-Min-Naing & Gatton, 2002). RDTs are relatively robust, simple to perform and interpret, and the interpretation of the results varies relatively little among the individual users. WHO (2000b) summarised comparative advantages and disadvantages between the light microscopy RDTs and they are presented in Table 1.6.

Table 1.6: Comparison of the requirements, performance, direct costs and technical specifications of microscopy and RDTs (WHO, 2000b)

	Microscopy	RDTs
Requirements		
Equipment	Microscope	None
Electricity	Preferred	None
Supplies	Blood collection, staining reagents and supplies, water	Blood collection, staining (supplied in some kits)
Training	Trained microscopist	Minimal training
Performance		
Test duration	Minimum 60 minutes	15-20 minutes
Labour intensiveness	High	Low
Subjectivity	High	Low
Robustness	Average	High
Direct costs		
Cost per test	0.12-0.40 USD	0.60-2.60 USD
Technical specifications		
Detection threshold	5-10 parasites/µl of blood	40-100 parasites/µl of blood
Quantification	Possible	Not possible
Differentiation between non-*P. falciparum* species	Possible	Not possible
Differentiation between sexual and asexual stages	Possible	Not possible
Detection of *P. falciparum* sequestered parasites	No	Yes
Antigen persistance	Not applicable	Some RDTs

RDT = rapid diagnostic test

1.4.4 Public health importance of malaria diagnosis

Misdiagnosis remains a major contributor to malaria morbidity and mortality (Ghebreyesus *et al.*, 1999); therefore, an early and accurate diagnosis is a key element of effective malaria case management (WHO, 2000a). However, the two diagnostic approaches traditionally used, clinical and microscopic malaria diagnosis, are not anymore entirely satisfactory. As described previously, clinical diagnosis inevitably results in overdiagnosis and overtreatment of malaria. This has been an acceptable and cost-effective practice during the era when cheap and safe first-line drugs, such as chloroquine and sulfadoxine-pyrimethamine were highly effective. However, the

introduction of new, more expensive and more complex to use drugs such as Artemisinin-based combination therapies (ACT), challenge the appropriateness of clinical diagnosis and increase the importance of minimising unnecessary drug use (WHO, 2001a). Furthermore, it has been argued that unnecessary use of antimalarial drugs may lead to the increased selection of drug-resistant parasites, however, this remains to be proven, since no data exist to date to quantitatively correlate patterns of drug use with the emergence of resistance.

Microscopic diagnosis of malaria has been seen as a potential tool to reduce the number of treated individuals but, in high malaria endemic areas, does not necessarily overcome the problem of asymptomatic, coincidental malaria parasitaemia in a febrile patient sick for another reason (Greenwood *et al.*, 1987; Armstrong-Schellenberg *et al.*, 1994). In Malawi, the introduction of microscopes into a hospital decreased significantly the number of unnecessary antimalarial prescriptions in adults and produced annual savings of 3% in the drugs budget for the hospital (Jonkman *et al.*, 1995). However, during the study in Malawi all clinicians strictly adhered to the recently introduced guidelines, prescribing antimalarial drugs only to the parasitaemic patients. In the studies performed under routine practice conditions in Kenya, Zambia, Benin and Tanzania, the introduction of microscopy did not change significantly the clinical diagnosis of malaria as 30-87% of patients with a negative blood slide still received antimalarial treatment (Barat & Kramer, 1999; Barat *et al.*, 1999; Holtz & Kachur, 2000; Makani *et al.*, 2003). Furthermore, it has been shown from several countries that the quality of malaria microscopy including the

accuracy of blood slide readings has been difficult to maintain in remote and poorly resourced areas (Durrheim *et al.*, 1997; Kachur *et al.*, 1998; Barat *et al.*, 1999).

The role of RDTs in Africa has been recently summarised by Bell (2004). The usefulness of RDTs in malaria case management will depend on whether the level of misdiagnosis can be reduced and the cost savings accrued by health services and patients. The cost-benefit ratios will depend on the cost of the RDT, the cost of the treatment, parasite prevalence, and the effect of the RDT on treatment practice. It is likely that the impact of RDTs would be higher in areas of lower malaria endemicity; if a high proportion of febrile patients have parasitaemia, the additional cost of diagnosis may not be recouped through the treatment saved. Similarly, the usefulness of RDTs is likely to be higher in malaria less-vulnerable adult patients where the incidence of disease is generally lower than in children (Snow & Marsh, 1998). Furthermore, the RDTs should overcome the problems experienced with microscopy where clinicians commonly ignore negative malaria slides. It is believed that the clinicians' confidence in malaria diagnosis using RDTs might be better maintained if the tests with high sensitivities are used and the quality assurance process is ensured from the procurement to the point of use (WHO, 2003b).

In conclusion, during an era of malaria case management where confirmatory diagnosis is urgently needed, malaria RDTs should be considered as a means of extending parasite-based diagnosis to areas where good quality microscopy cannot be maintained. However,

the cost-benefit impact of RDTs should be carefully evaluated in prospective, operational trials, randomised on the basis of the diagnostic strategy applied.

1.5. Malaria case management recommendations

Various international and national guidelines, clinical algorithms, wall charts and technical reports provide recommendations addressing specific components of malaria case management. Although the content and terminology used in different documents varies, the major components of the clinical process important for malaria case management can be classified into four areas: 1) clinical assessment, which includes history taking and clinical examination; 2) diagnosis, including the classification of malaria and the use of laboratory support; 3) effective treatment; and 4) adequate counselling and drug dispensing. Furthermore, some or all of the case management recommendations are commonly provided with regard to the particular patient groups (children, adults, pregnant women, travelers), intensity of malaria transmission (high endemic, low endemic, epidemic), severity of disease (uncomplicated, severe), type of management required (outpatient, inpatient, pre-referral) and level of care available (referral hospital, district hospital, peripheral health facility, facilities with available laboratory support, community level). Many of these classifications overlap and the terms are used interchangeably. In this section, the malaria case management recommendations presented focus broadly on the management of malaria at the outpatient, health facility level with the distinction of specific age groups where possible or appropriate.

1.5.1 Recommendations on the clinical assessment

The recommendations on the clinical assessment tasks are reflected in several international and national guidelines (Gove, 1997; MoH, 1998; 2000a; WHO, 1996a; 2003a). The primary goal of the evaluation of a patient with suspected malaria was distinguishing between uncomplicated and severe disease (WHO, 1996a). According to WHO, the assessment should include: 1) basic clinical examination (assessment of "*central nervous system function, including presence or history of convulsions and mental status*"; assessment of "*respiratory distress checking for respiratory rate, nasal flaring, chest indrawing, grunting, deep breathing and the use of accessory muscles of respiration*"; assessment of *hydration status;* assessment of *hyperpyrexia by measuring temperature;* and assessment of "*anaemia, either by laboratory testing or by clinical signs such as palmar, nailbed or conjunctival pallor*"); 2) assessment *of* "*whether the patient can take oral medications*"; and 3) determination "*whether the patient has received previous antimalarial treatment*".

Similarly, the Kenyan National Malaria Control Programme's (NMCP) guideline (MoH, 1998) emphasises early recognition of severe malaria in children recommending assessment of the following signs at the outpatient level: "*prostration (child cannot sit up if old enough or cannot feed in a younger child), impaired consciousness (using Blantyre coma scale) and respiratory distress (rapid deep breathing or chest indrawing)*". Very little is recommended by this guideline for the assessment tasks for uncomplicated malaria. The guideline states that "*history of clinical symptoms, previous drugs and travel*

should be taken to guide diagnosis and treatment of uncomplicated malaria at outpatient level".

The recent WHO guideline for the African Region (WHO, 2003a) is more specific with regard to uncomplicated malaria and recommends that the assessment should include a complete history of common malaria symptoms such as: "*fever, history of fever, chills, headache, joint pains and anorexia. In addition, the age, place of residence, recent history of travel, previous treatment and other illnesses should be noted. In children refusal to eat or feed, decreased activity and other symptoms may be present*". Furthermore, the patients with severe malaria should be assessed for "*extreme weakness, change in behaviour, convulsions, drowsiness, fast breathing, colour of urine, pregnancy, time of last drink or food*". The physical examination of the same patients should include the following assessment: "*palmar and conjunctival pallor (anaemia), behaviour change, coma and convulsions (cerebral malaria); sweating, weakness and cold skin (hypoglycaemia); pulmonary oedema and acidotic breathing (breathing difficulties); spontaneous bleeding from gums, skin and venepuncture sites; dark urine and yellowness of conjunctiva and palms (severe jaundice)*".

Malaria specific guidelines traditionally use a classified disease (uncomplicated or severe malaria) as an entry point to describe clinical features of malaria and provide the assessment recommendations. However, a major weakness of such approach, limiting its practical use as a job aide, is that patients do not present with classified disease but with

signs and symptoms either spontaneously reported by a patient, or requiring active identification by the health worker. This has been recognised by the IMCI guidelines.

Both the IMCI guidelines (generic and Kenyan specific) provide the most comprehensive and explicit recommendations with regard to the performance of the assessment tasks in children (Gove, 1997; MoH, 2000a). The IMCI uses an integrated approach to the sick child and specifies assessment tasks that should be performed for each sick and febrile child aged 2-59 months during their initial visit to a health facility. Among the other assessment tasks, each sick child should be assessed for palmar pallor, and the presence of the following general danger signs should be determined: "*if child is able to drink or breast feed, does the child vomit everything, has the child had convulsions and if the child is lethargic or unconscious*". The assessment of all febrile children (defined as history of fever, hotness of body or temperature ≥37.5°C) in the absence of any general danger signs should include: "*decision on malaria risk (high or low, based on an arbitrary threshold of 5% childhood fevers due to malaria); determination of duration of fever; every day presence of fever if fever present more than 7 days; presence of measles in the last three months; presence of stiff neck, runny nose and signs of measles*". Such an integrated approach to the sick child is not malaria specific, however, it assures systematic clinical assessment of most of the signs and symptoms related to severe malaria in children and provides a clear basis for further clinical decision making in the management of uncomplicated malaria.

In conclusion, various international and national malaria case management guidelines use different formats and terminology to provide recommendations with regard to the performance of assessment tasks. The content of recommendations are rarely harmonised between guidelines, the instructions are commonly ambiguous and incomplete, and clear and explicit assessment recommendations for adult patients are almost non-existent. The most explicit instructions are provided by IMCI guidelines; however, these guidelines only refer to the children below 5 years of age.

1.5.2 Recommendations on malaria diagnosis

Malaria diagnosis is a key element of malaria case management and all guidelines provide instructions on how malaria should be diagnosed in variety of clinical settings (Gove, 1997; MoH, 1998; 2000a; WHO, 1996a; 2000a; 2003a). Broadly, most of the guidelines differentiate recommendations for clinical malaria diagnosis from parasite-based diagnosis.

1.5.2.1 Recommendations for clinical malaria diagnosis

The IMCI guideline is the only one that does not advocate the use of microscopy and ignores its use in algorithms for the diagnosis of malaria in children at the outpatient level (Gove, 1997; MoH, 2000a). In areas of high malaria endemicity, IMCI recommends for all children aged 2-59 months during the initial visit, "*diagnosis of malaria based solely on the presence of fever (which includes history of fever, feels hot, or a temperature* $\geq$ *37.5°C)*". In low endemic areas, "*fever in the absence of measles, running nose or any other identifiable cause of fever*" presents a clinical indication to diagnose malaria. In

both areas of endemicity, if a child, previously diagnosed as having malaria, comes back to the facility for "*follow up visit with fever (persistent fever after 2 days or return within 14 days), malaria treatment failure is diagnosed in the absence of any cause of fever other than malaria*". A child presenting during initial or follow up visit with "*any general danger sign or stiff neck*", regardless of the level of malaria endemicity, should be classified as having "*very severe febrile disease*", should receive pre-referral management including antimalarial treatment and be sent to hospital urgently.

The WHO guideline for the African Region (WHO, 2003a) does not make any age distinction for diagnosis of uncomplicated malaria at peripheral facilities, uses an IMCI approach based on malaria risk and recommends that "*malaria should be clinically diagnosed in any patient who has fever or history of fever in the previous 48 hours in high malaria risk areas*"; while in low risk areas "*other causes of fever should be considered before treatment is started*". Furthermore, a clinical diagnosis of *severe* malaria should be made "*based on history, general danger signs and features of any of the signs of severe disease in the absence of signs of alternative diagnosis*".

Specifically for older children and adults, the latest WHO Expert Committee on Malaria (WHO, 2000a) suggests that in high endemic areas "*the sole criterion to diagnose malaria clinically in older children and adults is a history of fever, however absence of alternative explanation for the fever may be useful, especially in drawing attention to other conditions that may need to be treated*". The same committee states that in low endemic areas "*the absence of an alternative explanation of fever has been*

recommended, but there is need for more local clinical epidemiological research on specific criteria for the diagnosis of malaria". The Kenyan malaria specific NMCP guideline provides only a small section for children aged above 5 years and adults. In this age group clinical diagnosis of malaria is recommended in patients with *"fever or history of fever, chills, rigors, headaches, joint aches and pains in the absence of other causes of fever"* (MoH, 1998).

In summary, most of the recommendations for children below 5 years of age equate presence of fever with malaria diagnosis in areas of high malaria endemicity. In areas of low endemicity and in older children and adults regardless of the level of endemicity, it appears that all guidelines recognise the importance of identifying other causes of fever, yet none of them, with the exception of IMCI guidelines, clearly state how this criterion should be used and what signs and symptoms present an alternative explanation of fever.

1.5.2.2 Recommendations for parasite-based diagnosis

The majority of international and national malaria specific guidelines promote the use of microscopy wherever it is possible (WHO, 1996a; 2000a; 2003a; MoH, 1998). When microscopy is available, the diagnosis of uncomplicated malaria is commonly recommended for the patient presenting with *"history of fever and positive blood smear"* (WHO, 2003a), or in patients with *"parasitaemia and any of the clinical features of malaria and no sign of severe or complicated malaria"* (MoH, 1998).

However, the guidelines rarely specify clinical indications for the use of microscopy; some provide non-specific recommendations suggesting its use in case of clinical suspicion (WHO, 2003a), yet no guideline has provided explicit signs and symptoms indicating malaria microscopy in different patients groups or areas of endemicity. Furthermore, most guidelines are ambiguous with regard to the interpretation of blood smear results. For example, the Kenyan NMCP guideline states that *"in certain cases a slide may be negative even when the patient has malaria and conversely, malaria parasitaemia may not be the cause of the presenting illness"* (MoH, 1998). Similar recommendations can be found in international guidelines. The WHO guideline states that *"the presence of signs and symptoms of disease with negative blood smear does not preclude the diagnosis of malaria, particularly in endemic areas with high transmission"* (WHO, 2003a). Furthermore, not much clearer is the recommendation of the latest WHO Expert Committee on Malaria: *"Malaria disease may exist despite a negative microscopy result, but, unless the patient has already started treatment and there is a high suspicion of malaria, treatment for uncomplicated malaria should not be given, as long as microscopy is negative"* (WHO, 2000a).

Similar ambiguities are present in the WHO decision charts for diagnosis of malaria based on the results of malaria RDT (WHO, 2004). It has been specified that negative test result does not always exclude malaria and *"in case of high clinical suspicion patient should be treated for malaria while other illnesses should be excluded"*.

In summary, current international and national recommendations promote the use of parasite-based diagnosis, however, the messages conveyed to the clinicians on the role of microscopy and RDTs in malaria diagnosis are incomplete and ambiguous. Since the critical aspect for the success of any guideline is its clarity, its lack in most malaria case management guidelines represents their major limitation.

1.5.3 Recommendations on effective malaria treatment

The effective treatment of malaria is a cornerstone of malaria case management (WHO, 2000a). For nearly 50 years, chloroquine has been the bedrock of malaria case management in Africa. In Africa since the 1980s, the clinical efficacy of chloroquine declined rapidly (Talisuna *et al.*, 2004) and several countries, including Kenya, have replaced chloroquine with sulfadoxine-pyrimethamine (SP) as their first-line treatment for uncomplicated malaria. However, in recent years, in many areas of eastern and southern Africa SP resistance has been emerging rapidly (EANMAT, 2003; Talisuna *et al.*, 2004; Myint *et al.*, 2004).

As a response to increasing levels of antimalarial resistance, WHO currently recommends that all countries experiencing resistance to conventional monotherapies, such as chloroquine, SP or amodiaquine, should use combination therapies, preferably those containing artemisinin derivatives (ACTs) (Bosman & Olumese, 2004). WHO currently recommends the following therapeutic options:

1. artemether-lumefantrine,
2. artesunate plus amodiaquine,

3. artesunate plus sulfadoxine-pyrimethamine (for areas where SP efficacy remains high),
4. artesunate plus mefloquine (for areas with low transmission),
5. amodiaquine plus sulfadoxine-pyrimethamine (for areas where efficacy of both drugs remains high, mainly limited to countries in West Africa and only as short-term, interim treatment policy, while preparing to adopt an ACT).

Since 2001, twenty African countries, including Kenya, have adopted ACTs as first-line treatment for uncomplicated malaria, five countries adopted ACTs as second-line treatment while three countries have selected amodiaquine plus sulfadoxine-pyrimethamine as their first-line treatment (Olumese, 2004).

At present, quinine remains the recommended treatment for severe and complicated malaria. Of relevance for outpatient management, patients with severe malaria should receive intramuscular quinine and should be urgently referred for hospitalisation (MoH, 1998; 2000a; WHO, 2003a). Rectal artesunate is not yet officially recommended but presents a great potential for pre-referal management of severe malaria, particularly in areas where parenteral treatment would not be feasible (Barnes *et al.*, 2004).

Furthermore, an adequate antimalarial treatment does not include only an effective antimalarial drug but also provision of supportive treatment at health facility level. Several guidelines have addressed this issue and provided recommendations (Gove, 1997; MoH, 1998; 2000a; WHO, 2003a). Supportive treatment for malaria at outpatient level may include measures to reduce temperature such as tepid sponging, fanning and oral antipyretics, iron and folate for anaemia, intravenous or rectal anticonvulsants if

convulsions occur, or in case of low blood sugar concentrated glucose administered by nasogastric tube or by slow intravenous injection.

1.5.4 Recommendations on adequate drug dispensing and counselling

The most comprehensive recommendations on drug dispensing standards for treatment provided to sick children at the outpatient level are provided by IMCI guidelines (Gove, 1997; MoH, 2000a). Health workers should perform the following tasks for every oral drug to be given at home: "*determine the appropriate drugs and dosage for the child's weight or age; tell the mother the reason for giving the drug to the child; demonstrate how to measure a dose; watch the mother practice measuring a dose by herself; ask the mother to give the first dose to her child; explain carefully how to give the drug, then label and package the drug; if more than one drug will be given, collect, count and package each drug separately; explain that all oral drugs must be used to finish the course of treatment, even if child gets better; and check the mother's understanding before she leaves the clinic*".

Furthermore, IMCI guidelines recommend explicit counselling tasks to be provided to the caretakers of sick children. For example, children treated for malaria as outpatients should return to the health facility for "*follow up visit in 2 days if fever persists*". Any sick child, including children with malaria, "*should be breastfed more frequently and for longer at each feed*, or, *should be given increased quantity of fluids*" if child is not breastfeeding. All sick children should immediately return to the health facility "*if child becomes sicker or unable to drink or breastfeed*".

1.6 Quality of malaria case management

In this section the general concepts of the quality of care are introduced, the descriptive and interventional studies focusing on the quality of outpatient malaria case management are presented and methodological limitations of the studies on health workers performance are discussed.

1.6.1 Introduction to the general concept of the quality of care

The evaluation of the quality of case management focuses on performance according to standards because adherence to evidence-based standards is associated with improved health outcomes (Grimshaw & Russel, 1993). In a health systems view of care delivery, the standards can be applied to any of three components: structure (the conduit through which care is delivered, such as trained staff, equipment, supply), process (activities and tasks of actual care given, such as diagnosis and patient care management) and outcomes (the clinical consequence of care, influenced by the structure and the process) (Campbell *et al.*, 2000).

Donabedian (1980) suggests that the most direct approach to assessment of health care quality is to focus on the process of care and evaluate this against established standards. Furthermore, Gilson *et al.* (1995) argued that the priority in assessment of the quality of primary health care in developing countries is not an outcome component since primary health care is largely based on interventions for which effectiveness has already been demonstrated, therefore, it is more important to know why interventions are not properly

executed than to know their potential impact on the health status. The focus of discussion in this section will be the clinical process of care.

The standards of the clinical process of care can be presented in various formats such as clinical guidelines, algorithms, pathways, procedures, protocols or standing orders; however, a critical component of each standard is to contain explicit and measurable statements (Marquez, 2001). The performance according to standards can be measured using various direct and indirect methods, each of them having its advantages and disadvantages (Table 1.7).

Table 1.7: Methods for measuring performance according to standards, (Marquez, 2001)

Methods	Advantages	Disadvantages
Observation of service delivery (by expert observers, peers, supervisors)	• Greater validity	• Time-consuming • Requires careful standardization of observers to obtain reliable results • Some care activities are difficult to observe • Presence of observer may influence provider behavior
Simulated client	• Greater validity than indirect methods • Eliminates observation effect because health providers are not aware of being observed	• Time-consuming • Requires careful training and standardization of simulated clients • Some care activities are difficult to observe
Audit of individual patient records	• Inexpensive	• Records are often incomplete; tasks may have been performed but not recorded
Review of data from automated information system	• Inexpensive	• Data available through automated system may be very limited
Testing (written tests, simulation with standardized patients, computer-based testing)	• Affords greater consistency in presentation of cases	• Cannot evaluate interpersonal interactions
Health worker interview (self-report)	• Relatively quick and easy to implement	• Subject to bias due to inaccurate recall, not understanding the question, and the desire to appear competent
Patient exit interview (patient report, including by health workers themselves)	• Relatively quick and easy to implement	• Subject to inaccurate recall, lack of awareness of all the clinical tasks performed, failure to understand the question and the desire to provide the responses to please the interviewer
Measurement of patient outcomes linked to correct health provider performance	• Avoids observation effect	• Association between patient outcome and provider performance is only implied, not directly measured

1.6.2 Quality of outpatient malaria case management

There is overwhelming evidence that inadequate performance is strikingly widespread, as documented in studies of child health, sexually transmitted diseases, family planning, obstetrics, mental disorders, injuries, and diabetes (Rowe *et al.*, 2005). Maybe the most illustrative example was presented in 1993, when WHO reviewed data from surveys conducted in 28 countries with national training programs for the control of diarrhoeal diseases and they found that only 16% of children with diarrhoea were correctly assessed, and only 20% were correctly re-hydrated (WHO, 1993).

Despite the volume of the studies on health workers performance, comparatively few examined the quality of malaria case management. For example, in a methodologically rigorous review of the interventional studies to improve the use of antimicrobials in developing countries, only 6 of 52 studies included malaria as a target health condition, and of these 6, only 3 were published in peer-reviewed journals (WHO, 2001b). However, some information on the quality of various aspects of malaria case management is available from the descriptive studies undertaken using various study designs and analytical approaches. More structured data became available with the implementation of IMCI programme, which among other illnesses, addresses malaria under the broader management of the febrile child. In the following sections, clinical performance indicators from descriptive, baseline studies evaluating either outpatient malaria case management or malaria components embedded into IMCI guidelines are presented.

1.6.2.1 Performance indicators from descriptive malaria case management surveys

A variety of performance indicators were measured in several cross-sectional studies focusing on outpatient malaria case management. In Tanzania, Font *et al.* (2001) analysed all age patients routinely diagnosed with malaria and reported that 6% were weighed, 38% had temperature recorded, 24% had respiratory rate checked, 27% had conjunctival pallor checked, 3% had dehydration checked, 6% were given health education advice and 94% had an antimalarial drug prescribed, of which 10% were underdosed and 11% were overdosed. In Malawi, Lin & Franco (2000) reported that among children with fever the diagnostic process was adequate in only 18-42% of cases observed, a drug selected was correct in 71% of children but only 53% received the correct choice of drug, dosage, frequency and duration.

Studies of fever management across several countries showed that health workers failed to measure the patient's temperature in 10-54% of encounters, failed to ask about fever duration in 0-69% of encounters and ask about fever pattern in 36-90% of encounters (Nicholas *et al.*, 1991). On the Kenyan Coast, Abuya (2001) reported the performance of the following tasks among febrile children below 10 years of age: weight measured (4%), anaemia checked (65%), seizures assessed (27%), breaths counted (32%), malaria correctly diagnosed (72%), antimalarial treatment correctly prescribed (54%) and advice provided on treatment use (65%) and follow up (42%). In Western Kenya, Nyamongo & Oloo (2001) reported that 60% of patients were physically examined and that advice on the following was provided: vomiting (49%), follow up (27%) and immediate return to the facility (46%).

1.6.2.2 Performance indicators from the baseline IMCI surveys

More performance indicators related to outpatient malaria case management in children were revealed through a series of methodologically similar health facility surveys preceding the implementation of the IMCI programme (Lee, 1994; Herman, 1999; Kipera & Tsuma, 2000; Rowe *et al.*, 2000; 2001; 2003; Osterholt, 2002; Armstrong-Schellenberg *et al.*, 2004). The results of these surveys revealed that health workers rarely (<10%) assessed general danger signs or performed counselling tasks related to the child's follow up and immediate return to the facility (see Section 1.5 for definitions). Although the majority of these clinical skills were taught during the pre-service training and some during the various disease-specific in-service trainings, it was, however, not surprising that health workers without IMCI training rarely performed tasks presented for the first time in such a standardised and integrated format.

Despite the fact that health workers performance improved with regard to malaria diagnosis and treatment, frequent non-adherence to IMCI guidelines was more surprising since IMCI definitions reflected extensively promoted malaria case management standards such as presumptive diagnosis of all childhood fevers and prescription of recommended antimalarial treatment. Among patients with fever meriting diagnosis of uncomplicated malaria 67-92% of children were diagnosed as such by health workers (Lee, 1994; Herman, 1999; Kipera & Tsuma, 2000; Rowe *et al.*, 2001), and 45-84% of children with uncomplicated malaria had a recommended antimalarial drug prescribed (Lee, 1994; Kipera & Tsuma, 2000; Osterholt, 2002; Rowe *et al.*, 2000; 2003). However, in Uganda and Tanzania, where correct dosage of antimalarial drug was included in the

definition of correct treatment, only 24% and 25% of children with uncomplicated malaria were correctly treated respectively (Gouws *et al.*, 2004; Armstrong-Schellenberg *et al.*, 2004). Interestingly, within the same district in Kenya, prescription of the recommended antimalarial drug was only 14% in non-government health facilities (Herman, 1999) compared to 84% in government facilities (Lee, 1994). The summary of the results on correct malaria diagnosis and treatment is presented in Table 1.8.

Table 1.8: Correctness of malaria diagnosis and treatment from the health facility surveys assessing performance of health workers before IMCI training

Reference	Country	Year of survey	HF ownership	Age (months)	Correct diagnosis	Correct treatmen
Lee, 1997	Kenya	1994	Gov	2-59	79%	84%
Herman, 1999	Kenya	1999	Non-gov	2-59	92%	14%
Kipera & Tsuma, 2000	Kenya	2000	Mixed[a]	0-59	91%	68%
Rowe *et al.*, 2000	CAR	1995/96	Mixed[a]	2-59	NA	50%
Rowe *et al.*, 2001; 2003	Benin	1999	Mixed[a]	2-59	67%	63%
Osterholt, 2002	Malawi	1999	Mixed[a]	2-59	NA	45%
Gouws *et al.*, 2004	Uganda	2000	Gov	2-59	NA	24%[b]
Armstrong-Schellenberg *et al.*, 2004	Tanzania	2000	Gov	2-59	NA	25%[b]

[a] Mixed category includes government and non-government facilities
[b] Not pre-interventional, baseline survey, but data from comparison districts without IMCI training
HF = health facility; **NA** = information not available; **CAR** = Central African Republic; **Gov** = government; **Non-gov** = non-government

1.6.3 Improvements in the quality of malaria case management through IMCI programme

In this section the improvements in the quality of malaria case management as a result of the interventions related to the implementation of IMCI programme are presented. In Bungoma and Vihiga districts in Kenya, between 1994 and 2002, a series of health facility surveys around multiple, IMCI related interventions have been performed. Herman (2003) comparatively summarised the performance indicators from three surveys, undertaken in the following years: 1994 (before IMCI training), 1997 (following

IMCI training and implementation of the strengthened supervision), and 2002 (following package of interventions including site visits by senior staff, non-monetary incentives and provision of IMCI clinical registers). Herman (2003) demonstrated consistent improvements over time across all performance indicators assessed, especially those related to assessment and counselling, but also observed that, in spite of study limitations, no single intervention was associated with improved performance. Table 1.9 presents a comparative evolution of the performance indicators in Bungoma and Vihiga districts of relevance for malaria case management.

Table 1.9: Comparison of malaria related performance indicators between 1994 baseline, 1997 and 2002 health facility surveys in Bungoma and Vihiga districts in Kenya (Herman, 2003)

Performance indicators	1994[a] (%)	1997[a] (%)	2002[b] (%)
Assessment of three general danger signs[c]	0	42	73
Assessment of fever	83	93	97
Assessment of palmar pallor	5	73	88
Correct diagnosis of very severe febrile disease	0	11	59
Correct diagnosis of severe anaemia	0	11	20
Correct diagnosis of non-severe malaria	79	91	93
Correct diagnosis of moderate anaemia	3	21	37
Correct treatment of very severe febrile disease	13	48	63
Correct treatment of non-severe malaria	84	95	90
Correct treatment of moderate anaemia	1	16	41
Advise to return immediately if the child becomes sicker	8	56	69
Advise to return immediately if child unable to drink/breastfeed	NA	37	38
Advise caretaker to continue feeding or breastfeeding	NA	48	58
Advise caretaker to give extra fluids	NA	33	54

[a] 1994 and 1997 surveys performed in government health facilities in both districts
[b] 2002 survey performed in government and non-government facilities in Bungoma district only
[c] It includes asking if child unable to drink or breast feed, vomiting everything and convulsions
NA = information not available

In Tanzania, Armstrong-Schellenberg *et al.* (2004), as part of the multi-country evaluation of IMCI, compared the quality of case management between districts that implemented IMCI through the standard 11 days course for health workers and comparison districts without IMCI activities. The authors concluded that children in IMCI districts received better care than children in comparison districts: they were more thoroughly assessed, they were more likely to be diagnosed correctly and strikingly better performance was demonstrated with regard to treatment, drug administration and counselling.

However, compared to Tanzania, the effects of the IMCI training on health workers performance was significantly lower in a similar type of evaluation in Uganda (Gouws *et al.*, 2004). Possible explanations provided by Gouws *et al.* (2004) was that IMCI programme in Uganda was less controlled, the quality of training, supervision and follow up may have been of lower quality and the effect may have been diminished by the abolition of user fees and existing low morale of health workers. Table 1.10 presents several performance indicators related to the appropriateness of antimalarial treatment and advice given to caretakers by health workers with and without training in IMCI in Tanzania and Uganda.

Table 1.10: Comparison of malaria related performance indicators between health workers with and without training in IMCI in Tanzania (Armstrong-Schellenberg *et al.*, 2004) and Uganda (Gouws *et al.*, 2004)

	Tanzania		Uganda	
Performance indicators[a]	**IMCI trained (%)**[a]	**Not trained (%)**[a]	**IMCI trained (%)**[a]	**Not trained (%)**[a]
Child needs antimalarials and receives correct prescription	85	25	49	24
Child receives the first dose of treatment at the facility	84	1	21	3
Caretaker of child who is prescribed antimalarials ia advised how to use them	96	13	46	22
Caretaker of sick child is advised to give extra fluids and continue feeding	90	4	NA	NA
Sick child whose caretaker is advised on when to return immediately	66	1	NA	NA

[a] All country-specific differences statistically significant at 5% level of significance
NA = information not available

1.6.4 Determinants of the quality of malaria case management

In several cross-sectional health facility surveys, rigorous multi-level methods of analysis were applied and a variety of health facility, health worker, patient and consultation factors influencing health worker performance, and in particular the quality of treatment provided to children with uncomplicated malaria, were examined (Rowe *et al.*, 2000; 2001; 2003).

In Benin, Rowe *et al.* (2001; 2003) examined a range of health worker performance outcomes and reported that various in-service trainings, including the malaria specific one, were not associated with any of the measured performance outcomes including the quality of treatment for uncomplicated malaria. Indeed, the only association found was the higher likelihood of trained health workers in diarrhoea management to pinch the skin of a child to assess for dehydration (Rowe *et al.*, 2001). Similarly, results from Central African Republic did not show an association between malaria in-service training and

prescription of the correct treatment for children with fever (Rowe *et al.*, 2000). It appears that these findings are consistent with a less rigorous interventional trial in Ghana, where it was suggested that malaria in-service training improved health workers knowledge of the clinical management of the disease, however, the effect of knowledge improvement was not translated into better clinical practice over the longer term (Ofori-Adjei & Arhinful, 1996).

Similarly, studies in Benin and Central African Republic did not show an association between health workers' supervision, possession of guidelines, and the various performance outcomes including the correct treatment for uncomplicated malaria (Rowe *et al.*, 2000; 2001; 2003). It appears that results on the effects of guidelines in these studies are consistent with findings from developed countries where educational materials alone have little or no effect at all on performance according to standards (Marquez, 2001). With regard to the effect of wall charts on correct treatment for uncomplicated malaria conflicting results were reported; in Benin the presence of wall charts was associated with better performance (Rowe *et al.*, 2003) and in Central African Republic the wall charts were associated with more treatment errors (Rowe *et al.*, 2000).

The findings of these studies should not imply that malaria in-service training or supervision are ineffective as a strategy, however given the common lack of qualitative details on training and supervision, it may have been that such interventions were simply insufficient or inadequate in the study settings (Rowe *et al.*, 2003). This may explain why evaluations within the more robustly implemented IMCI programme, which frequently

includes standardised follow up and supervisory visits, have demonstrated the positive effect of in-service training on health workers performance (Naimoli, 2001; Herman, 2003; Gouws *et al.*, 2004; Armstrong-Schellenberg *et al.*, 2004).

The findings of previous studies can be complemented by a review summarising interventional trials testing the effects of in-service training and supervision on broader drug prescribing practices for a variety of health conditions (Ross-Degnan *et al.*, 1997). With regard to training, of 14 studies meeting strict methodological criteria, 3 achieved large improvements, 7 showed moderate effects and 4 had little impact; however, 2 of 3 high impact interventions did not measure actual change in practice. However, it has been shown that supervision can improve pharmaceutical use of drugs in primary care in developing countries in the short term (Ross-Degnan *et al.*, 1997). In the long term, if correctly done, it could be a mechanism for providing professional development and increasing motivation and job satisfaction (Rowe *et al.*, 2005).

1.6.5 Methodological limitations of the studies on health workers performance

Studies of health worker performance suffer from multiple limitations and the major ones are presented in this section. First, in developing countries, randomised control trials as "gold standard" investigations to test the effect of a determinant or an intervention on health worker performance, are rarely performed. However, if rigorous methods are used and careful interpretation of results is applied, trials with time-series or pretest-posttest study designs, or cross-sectional surveys, can provide useful data on what happens under real life conditions (Rowe *et al.*, 2005). Qualitative research methods may complement quantitative results and help to better describe contextual factors, sophisticated aspects of

interventions and latent variables such as motivation (Victora *et al.*, 2004). Second, the studies on health worker performance, and especially those not appearing in peer-reviewed journals, are frequently poorly documented with unavailable and inadequate explanation of the research methods. Third, description of the tested interventions or determinants is frequently incomplete or confusing, making it difficult to determine to what the observed effects should be attributed. Fourth, the sample sizes are frequently small, non-probability samples and this is rarely accounted for in the analysis. For example, non-probability samples occur when health facilities are sampled from the sampling frame with unequal probability of selection or when within the facility only limited number of observations is performed during the clinical service delivery day. Fifth, data collection techniques related to patient-provider clinical interaction are mostly based on observation-based methods and rarely complemented with exit examination to present "gold standard" diagnosis and determine with greater confidence the appropriateness of health workers practices. Sixth, the observation of patient-provider clinical interactions has the limitation that the presence of the study observer may cause the health workers to perform better or worse than usual (the Hawthorn effect); however, there is no perfect method since the other commonly used techniques such as review of patient records or simulated clients suffer from other disadvantages (Table 1.7). Seventh, in many studies only a narrow range of potential determinants has been investigated and when multiple factors were examined an attempt to adjust for confounding by using multivariate techniques has rarely been made. Eighth, the data collected in health facility surveys are cluster-correlated and multi-level in nature (numerous clinicians seeing multiple patients within different facilities); statistical analysis failing to account for the

similarities within the cluster may result in an underestimation of variance and increased type I error rate. Ninth, health workers performance results may be difficult to interpret when standards are not in the form of explicit or measurable statements, or the outcome measured does not indicate if the performance is appropriate (i.e. percentage of all patients with antimalarial prescribed).

1.7 Kenyan context

This section describes the basic Kenyan health system context, the setting of the thesis and focuses on the importance of adequate malaria case management within the current malaria control activities specified in the National Malaria Strategy. The section further discusses the role of malaria case management within the context of new antimalarial drug policy change.

1.7.1 Location and basic health indicators

Kenya is located in East Africa and shares borders with Uganda to the west, Tanzania to the south, Ethiopia to the north, Sudan to the northwest, Somalia to the east, and the Indian Ocean to the south-east. The country lies between latitudes 5°00'N and 4°40'S; and between longitudes 33°83'E and 41°76'E, covering the surface of approximately 580,367 km^2 (Ojany & Ogendo, 1988). The country is divided into five administrative levels; there are eight provinces sub-divided into 70 districts that are further divided into divisions, locations, and sub-locations. In 1999, Kenya had a population of approximately 29 million persons, of whom 44% were aged below 15 years, 52% were between 15 and 64 years and 4% were 65 years and above (CBS, 2001).

The health status of Kenyans improved significantly from independence in 1963 until the early 1980s, however, since the early 1990s a decline has been observed. Between independence and the early 1980s the annual infant mortality rate was reduced from 119 to 58 deaths per 1000 live births (MoH, 2004a; NCPD, 1989); likewise, mortality among children under five years of age had dropped from 106 in the 1970s to 89 in 1989 (NCPD, 1994). Both indicators showed evidence of an increase by the early 1990s (NCPD, 1989; 1994; 1999), and in 2003, infant and childhood mortality reached levels of 78 and 114 deaths per 1000 live births respectively (CBS, 2003).

1.7.2 Basic description of the formal health system in Kenya

Formal health services in Kenya are provided through government (GoK), non-government (NGO), local authority, mission, and private health facilities. Noor *et al.* (2004) estimated that there were 6,674 health facilities in Kenya in 2004; the GoK run approximately a third of these facilities, a further 18.2% were run by the mission and NGO sector, 1.4% by local authorities and 44.2% of facilities belonged to the private sector. GoK health facilities are organised through a pyramidal network of providers, starting with dispensaries at the lowest level of service, followed by sub-health centres, health centres, rural training health centres, sub-district hospitals, district hospitals, provincial general hospitals, and finishing with a facility of the highest level, the Kenyatta National Hospital (Owino, 1997).

Facilities become increasingly complex in diagnostic, therapeutic and rehabilitative services at the upper levels, which serve also as the referral levels (Owino, 1997; Noor *et*

al., 2004). At the district level, although the GoK facilities are nominally categorised as described above, in reality with regard to the services provided, there are difficulties distinguishing between various levels of service, such as dispensaries versus sub-health centres or rural health training centres versus sub-district hospitals. However, as a general rule, outpatient services are provided at facilities at all levels while the limited provision of inpatient services starts at the level of health centres (Noor *et al.*, 2004). At dispensary and health centres, most of the outpatient services are provided by enrolled and registered nurses whose 3 and 4 year of nursing training respectively includes the management of the most common conditions. In hospitals, clinical officers with a three-year diploma in clinical medicine are the major providers of outpatient services.

1.7.3 Burden of malaria in Kenya

Kenya has a diverse ecology that supports the entire range of stable and unstable *P. falciparum* transmission conditions (Snow *et al.*, 1998b). To describe malaria transmission intensities in Kenya, Snow *et al.* (1998b) used 124 cross-sectional, childhood (0-10 years), community-based malaria prevalence surveys measuring parasite ratios (PR) and broadly classified malaria endemicities into high (PR ≥70%), moderate (PR 20-69%) and low (PR<20%) areas of transmission. Furthermore, to model the risk of malaria morbidity and mortality across various intensities of malaria transmission the authors attributed Kenya climate data, 1989 population census figures, and demographic surveillance data from across Africa using verbal autopsy method with known accuracy errors (Snow & Marsh, 1992; Todd *et al.*, 1994; Anker, 1997; WHO, 1999).

Results indicated that in 1997, approximately eight million people were exposed to unstable malaria and five million were exposed to a low risk of stable transmission in Kenya. Over 11 million people were estimated to be exposed to moderate levels of *P. falciparum* transmission and about four million people including 677,000 children lived under areas of high transmission intensity. The authors concluded that in 1997 in Kenya, approximately 26,000 malaria deaths may have occurred among children aged less than five years and that approximately 145,000 children aged 0-4 years would have been hospitalised for severe malaria. The figures increase with epidemics in epidemic-prone and low risk arid areas of Kenya (Table 1.11).

Table 1.11: Populations exposed to risk of different malaria endemicities in Kenya and risk estimates for malaria mortality and morbidity (Snow *et al.* 1998b)

Feature	Unstable Rainfall Limiting	Unstable Non-rainfall	Low Stable (PR < 20%)	Moderate Stable (PR 20-69%)	High Stable (PR ≥70%)
1997 total population	680,247	7,834,477	4,945,381	11,113,368	3,737,639
1997 0-4 years population	115,961	1,375,255	848,946	1,960,626	677,006
Malaria mortality per 1000 children 0-4 years p.a.	0 (29-125)[a]	0.55	0.55	9.33	9.77
Numbers of deaths 0-4 years p.a.	0 (3,363-14,495)[a]	756	467	18,293	6,614
Malaria admission rates per 1000 children 0-4 years p.a.	-	21.38	21.38	38.58	32.30
Expected malaria admissions 0-4 years p.a.	-	29,403	18,150	75,641	21,867

[a] In epidemic year; **PR** = parasite ratio; **p.a.** = per annum

1.7.4 Kenyan National Malaria Strategy

The Ministry of Health's Division of Malaria Control (DOMC) is the operational arm of the National Malaria Control Programme and is responsible for overseeing the implementation of the Kenya National Malaria Strategy (KNMS). The KNMS was launched in April 2001 with the main objective to reduce the level of malaria mortality in

Kenya by 30% by the year 2006, and to sustain that improved level of control to 2010 (DOMC, 2001).

The KNMS has four main pillars of disease control that are congruent with those of the RBM initiative (www.rbm.who.int, accessed 15/01/2005; DOMC, 2001). The four pillars comprise the following:

1. *Clinical management: providing effective and prompt treatment*
2. *Management of malaria and anaemia in pregnancy*
3. *Vector control using insecticide treated bed nets (ITN) and other methods*
4. *Epidemic preparedness and response*

These four pillars are supported by two crosscutting strategies: "*Information, Education, and Communication*" and "*Monitoring, Evaluation and Research*".

1.7.4.1 Clinical management as the first pillar of the KNMS

With regard to the first pillar - clinical management - the KNMS presents the set of policies made to ensure that:

1. *All fevers are treated as early and as close to a patient's home as possible, with acceptable quality and correct dosages of the first-line antimalarial and supportive treatment.*
2. *First-line therapeutic failures will be appropriately referred and managed with recommended second-line treatment.*
3. *All complications of malaria will be referred and managed according to national guidelines.*

The KNMS specifies a series of mid-term clinical management targets to be achieved by the year 2006, and they are the following:

1. *80% of households at risk will receive targeted IEC materials*
2. *80% of Government of Kenya facilities will have continuous and adequate supplies of drugs essential for the management of malaria*
3. *80% of all antimalarial drugs provided through formal and informal sectors will be of internationally acceptable standard of quality*
4. *60% of all fevers which are treated at home by family members or caretakers will be managed appropriately*
5. *80% of all cases of fever treated by community health workers or outpatient facilities will be managed according to national recommendations*
6. *80% of first-line therapeutic failures and severe, complicated malaria cases will be correctly managed by health personnel in appropriate health facilities.*

To achieve the above targets, the implementation of the policies within the clinical management pillar emphasises the improvement of malaria case management and monitoring of drug efficacy among other activities (DOMC, 2001). The proposed activities aiming at the improvement of case management include development and dissemination of malaria case management guidelines and provision of pre-service and in-service training activities. Between 1998 and 2000, two national malaria specific case management guidelines were developed: "*National Guidelines for Diagnosis, Treatment & Prevention of Malaria for Health Workers*" (MoH, 1998) and "*A Simplified National Guideline on Malaria Control for Community Resource Persons* (MoH, 2000b), and malaria component of the IMCI guideline has been finalised and incorporated into the broader IMCI algorithms (MoH, 2000a). Between 1999 and 2001, 12,000 and 80,000 copies of the malaria specific guidelines for health workers and community resource persons were disseminated to a wider spectrum of health service providers respectively (Snow *et al.*, 2001a).

Furthermore, the DOMC partnered with a number of organisations to undertake a series of in-service training programs around malaria case management in support of the produced malaria specific guidelines. Between 1999 and 2001, the Mission for Essential Drugs, the African Medical Research Foundation, *Médecins Sans Frontières*, MERLIN, PLAN International, and the DOMC undertook various in-service training programs. It has been estimated that approximately 2,800 health workers had been trained by the end of 2001 nationwide (Snow *et al.,* 2001a). However, by 2001 the implementation of the IMCI programme was still in the nascent stages and only 3 districts had been covered with IMCI training.

In 1998, following the change of the national antimalarial drug policy and abandoning of chloroquine, the East African Network for Monitoring Anti-malarial Therapy (EANMAT) was established and eight sentinel sites were determined to monitor first-line and second-line antimalarial drug efficacy in Kenya. Between 1998 and 2004, the first-line antimalarial drug recommended for use in Kenya was sulfadoxine-pyrimethamine (SP) with amodiaquine and oral quinine reserved as second-line treatment (MoH, 1998). However, resistance to SP emerged rapidly (EANMAT, 2001; 2003) and Kenya was faced with no option but to change first-line therapy once again. This time, following advice from WHO and the international research community, artemisinin-based combination therapy (ACT) was adopted (WHO, 2001a). After careful consideration of the limited ACT options artemether-lumefantrine (ART-LUM) was selected as the only adequate choice for Kenya and in April 2004 the new first-line policy for uncomplicated malaria recommending ART-LUM was adopted (MoH, 2004b).

1.7.5 Importance of adequate malaria case management within the ACT drug policy

There is a substantial difference between the new era of ACTs and the era when cheap and simple to administer first-line drugs such as chloroquine and SP were effective against malaria. Effectiveness of ART-LUM treatment will differ from the efficacy in a number of ways and one of the most important determinants may be the effect of adherence. ART-LUM has a complicated 6-dose treatment schedule and an unfavorable pharmacokinetic profile; a poor level of oral bioavailability characterises lumefantrine, absorption varies considerably between individual doses and between patients, and absorption is significantly reduced in the acute phase of malaria (White *et al.*, 1999; Ezzet *et al.*, 2000). Therefore, from the health worker perspective, adequate performance in drug prescribing, patient's counselling and drug dispensing will be of critical importance to ensure optimum effectiveness of ART-LUM treatment.

Furthermore, a subsidised cost of 2.4 USD for an adult treatment course with ART-LUM (WHO, 2003c) is still thirty-fold higher than the cost of the previous treatment with SP (http://erc.msh.org, accessed 15/01/2005). In a country with limited financial resources such as Kenya, despite the promising commitments from external donors, it is reasonable to believe that a previously tolerated strategy of presumptive treatment of all fevers as malaria should be reconsidered. The change of malaria diagnosing practices intending to reduce number of treatments, either by introducing parasite-based diagnosis or by applying clinical criteria, will require strengthening of malaria case management with a particular focus on the adequate performance of clinical assessment tasks, use and interpretation of diagnostics, and adequate differential diagnoses.

Therefore, the quality of malaria case management is a critical component of any malaria control strategy, however, given the importance of treatment as a cornerstone of malaria case management, the significance of health workers performance will become even more pronounced in the era of ACTs. Many lessons can be learned by examining the current health workers practices and understanding factors influencing them. This thesis is aimed at contributing to this body of evidence and will hopefully lead to the development and implementation of improved malaria case management strategies.

1.8 The scope of the thesis

Chapter 1 describes the basic biology of malaria transmission, the measures and distribution of malaria endemicity and population with the focus on sub-Saharan Africa. The chapter then describes the clinical presentation of malaria and the epidemiology of malaria disease in relation to the acquisition of the functional immunity. It continues with a detailed section on malaria diagnosis, elaborating on difficulties of clinical diagnosis of malaria, parasite-based diagnostic methods and the public health importance of malaria diagnosis. The subsequent sections present international outpatient malaria case management recommendations, introduce the concept of the quality of care and presents the studies and limitations of health worker performance research with a focus on malaria case management. The chapter ends with the basic description of Kenyan context and the national malaria strategy, highlighting the importance of malaria case management.

Chapter 2 describes the materials and methods used to capture empirical data for each of two separately undertaken, age-specific health facility surveys. The chapter provides detailed information about study areas, national malaria case management standards and definitions used in the analysis, sampling procedures, data collection tools, training of the field workers, health facility survey procedures, statistical analysis performed and methodological limitations encountered.

Chapter 3 presents descriptive results on the quality of the outpatient malaria case management in children below 5 years of age. The chapter starts with a short introduction to the topic of the chapter, presents performance data for each component of the clinical process (assessment, diagnosis, treatment and counselling), describes health worker and health facility characteristics considered important for adequate performance of malaria case management and ends with discussion on the significance of the findings in the Kenyan context[1].

Chapter 4 presents the predictors analysis of multi-level variables (health facility, health worker, and patient or consultation) in relation to national treatment recommendations for uncomplicated malaria in children. The analysis uses recent statistical approaches applying multiple binomial logistic regression modeling for three categories of treatment quality (recommended, minor errors, and inappropriate). The chapter ends with a

[1] Some results from Chapter 3 have been published in *Annals of Tropical Medicine and Parasitology;* see details in bibliography under Zurovac *et al.* (2005).

comparative discussion of the determinants of health workers' performance between studies with a similar design[2].

Chapter 5 focuses on older children and adults, providing a short introduction to the topic and then proceeds to present the thesis data on the accuracy of the routine clinical diagnosis of malaria, the health workers practices in clinical assessment of febrile patients, and the ability of clinical signs and symptoms to predict malaria infection in febrile patients. The chapter ends with discussion and the implications of study findings on present and future national antimalarial drug policies.

Chapter 6 focuses on the effects of microcopy on malaria case management in Kenya. The chapter provides a short introduction to the topic, presents observational data collected on current clinical and laboratory practices from the facilities with functional microscopy, and discusses the current effectiveness of malaria case management using microscopy and the implications of the results on malaria diagnostic strategies in Kenya.

Finally Chapter 7 provides a summary of the thesis emphasising the major findings, overall importance of the findings in Kenyan context and identifies some of the areas that demand further investigation.

[2] Chapter 4 has been published in *International Journal of Epidemiology;* see details in bibliography under Zurovac *et al.* (2004).

CHAPTER 2:

Background, materials and methods of health facility surveys

2.1 Background

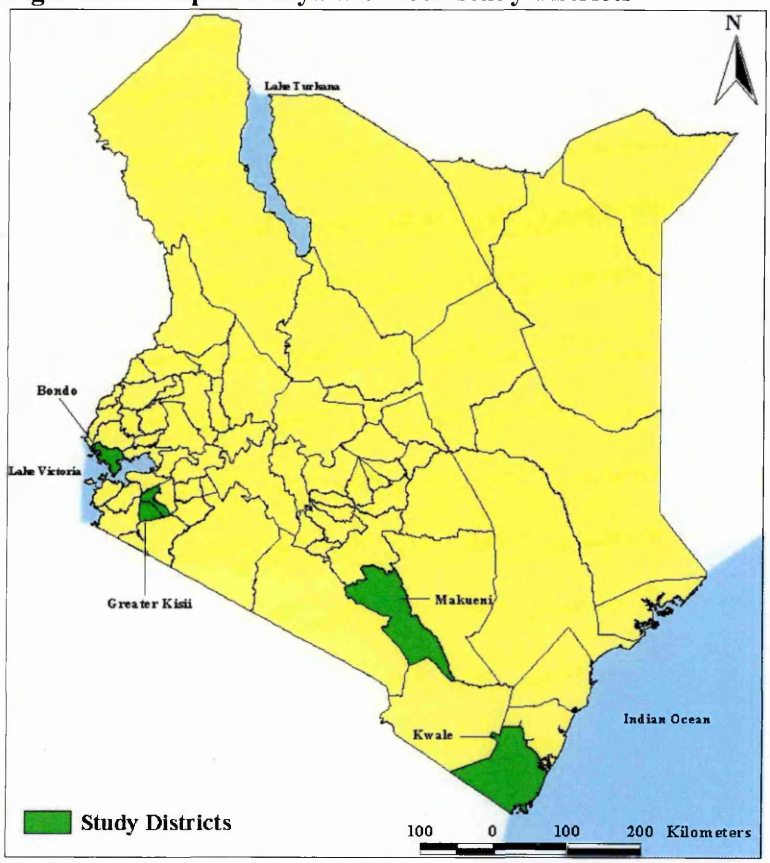
This chapter describes the materials and methods adopted for two separate health facility surveys, undertaken for children below 5 years and patients above 5 years. The chapter provides detailed information about the study areas, national malaria case management standards and definitions used in the analysis, sampling procedures, data collection tools, training of the field workers, health facility survey procedures, statistical analysis performed and methodological limitations encountered.

2.2 Background on the selection of the study districts

The Kenyan Ministry of Health's (MoH) Division of Malaria Control (DOMC) has identified four districts across the country as sentinel sites for prospective monitoring and evaluation of national malaria control activities at community and health facility level, including monitoring of antimalarial drug sensitivity at already existent sites identified by the East African Network for Monitoring of Antimalarial Treatments (EANMAT). Furthermore, these four districts were purposively selected because they represent the four principal malaria ecologies in Kenya and they were: Kwale (coastal environment with moderate to high transmission), Bondo (lakeside environment with perennial high transmission), Kisii comprising Kisii Central and Gucha (highland environment with highly seasonal transmission) and Makueni (semi-arid environment with acutely seasonal, low intensity transmission) (Figure 2.1.). From the national DOMC perspective these four districts were programmatically equally treated as any other district in Kenya, however, the health systems differences such as number of health facilities have existed between the selected districts. The studies of this thesis were developed in collaboration

with the DOMC and therefore took place in four districts previously identified for monitoring and evaluation activities.

Figure 2.1: Map of Kenya with four study districts



2.3 Characteristics of the study districts

2.3.1 Bondo district

Bondo district is one of the twelve districts in Nyanza Province. The district lies between latitude 0.400^0 south to 0.05^0 north and from longitude 33.967^0 to 34.433^0 east, and covers a surface of 987 km². Along its western border lies Lake Victoria. In 1999, the district had a population of 238,780 people and a density of 242 persons per km^2 (CBS, 2001). The population are predominantly JaLuo (95%). In Kenya, mortality rates are not

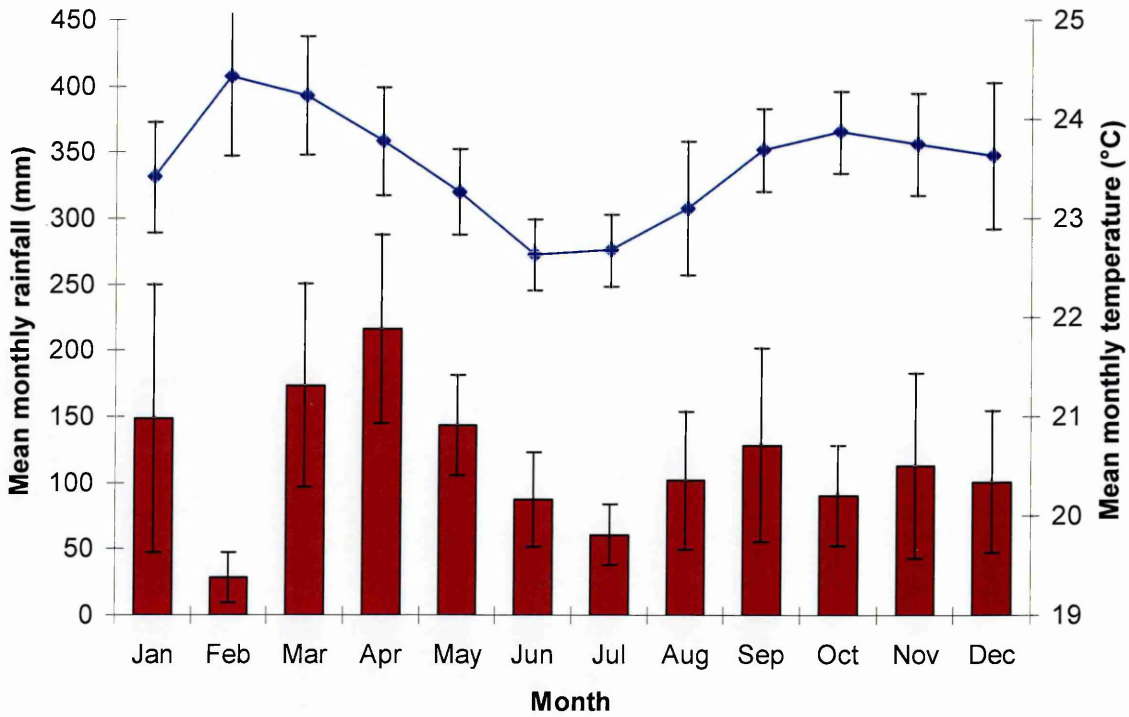
available at district level; however, infant and childhood mortality rates of 176 and 257 per 1000 live births respectively were reported from Asembo Bay Division of Bondo district (McElroy *et al.*, 2001). A nutritional survey undertaken in Bondo and Siaya districts in 1994 among 138 children aged 6-59 months showed that 33.8% of children were stunted, 3.8% wasted and 15.8% were undernourished (CBS, 1994).

2.3.1.1 Climate characteristics

Rainfall and temperature data are not available for Bondo district, however, to describe climatic characteristics of the district, data from neighbouring Kisumu district, harbouring a similar malaria ecology and located on Lake Victoria were used. Daily data on rainfalls and temperature were collected from Kisumu Meteorological Station for the time period between 1998 and 2003. The mean monthly rainfall and the mean monthly temperature were calculated for the period 1998-2003 and are presented in Figure 3.2. The mean monthly rainfall between 1998 and 2003 was calculated for each of 12 calendar months by adding quantity of rainfalls for particular month and dividing the total by 6 years examined. The total annual rainfall in the same time period ranged from 1216 to 1618 mm/year with a range of 4 to 317 mm of rain a month. The rains occur throughout the year, however, the long rains usually fall between March and May, and short rains have their peaks in September and January. The mean monthly temperature for each month between 1998 and 2003 was calculated from the mean monthly maximum and minimum temperatures for the respective months. The mean monthly temperature between 1998 and 2003 was calculated for each of 12 calendar months by adding mean monthly temperatures for particular month and dividing the total by 6 years examined.

Between 1998 and 2003, the average monthly maximum temperature was 29.9°C with a monthly range of 28.6-31.6°C, and the average monthly minimum temperature was 17.2°C with a monthly range 16.6-18.1°C. The month of February, just before the long rains, is the hottest month of the year while the coolest month is June at the end of the long rains (Figure 2.2.).

Figure 2.2: Mean monthly rainfall (bars) and mean monthly temperature (line) with intervals presenting one standard deviation around the monthly means: data from Kisumu Meteorological Station, Kisumu district, 1998-2003

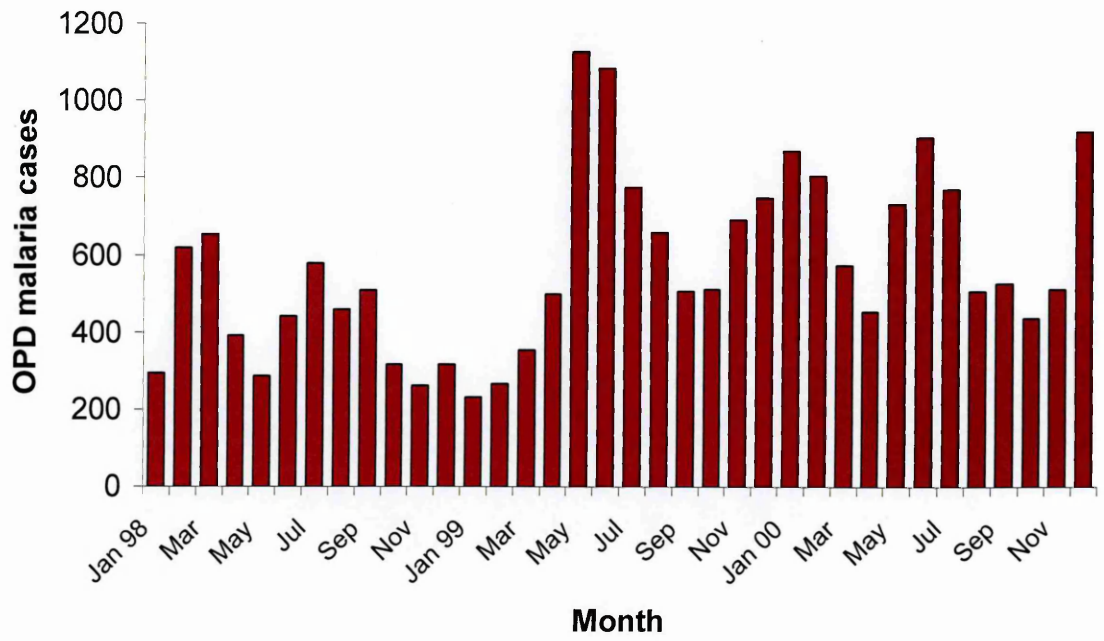


2.3.1.2 Seasonality of malaria transmission

In Bondo district malaria transmission is present throughout the year and is considered as stable and intense with estimated average of 0.75 infective bites per person per day (Beier *et al.*, 1994). However, a seasonal increase of malaria cases usually occurs between May and July, and between December and February. The increase in malaria cases usually

lasts three months and starts one month after the beginning of the rainy season. The paediatric survey in Bondo district was conducted in the month of October. The example of a consecutive series of monthly, outpatient, all age malaria diagnoses reported from Bondo District Hospital between January 1998 and December 2000 demonstrates the pattern of malaria seasons in the district (Figure 2.3.).

Figure 2.3: Consecutive series of monthly, outpatient, all age malaria diagnoses, Bondo District Hospital, January 1998 - December 2000



2.3.1.3 Age structured profile of outpatient malaria diagnoses

The age structured, monthly, outpatient malaria diagnoses were collected from 6 health facilities in Bondo district between 1998 and 2000 (Table 2.1). The age-specific distribution of malaria diagnoses shows that 19.3% (range 10.0-23.4%) of malaria diagnoses were reported in children less than one year, 25.3% (range 14.1-30.2%) in age group 1-4 years and 12.0% (range 8.8-18.2%) in age group 5-14 years. Patients older than 14 years accounted for 42.8% (range 36.5-60.2%) of malaria diagnoses.

Table 2.1: Distribution of malaria diagnoses across age groups: results from 6 health facilities in Bondo district between 1996 and 2001

	No of months[a]	< 1 year (% total)	1-4 yrs (% total)	5-14 yrs (% total)	< 5 yrs NS (% total)	≥ 15 yrs (% total)	Total
Bondo District Hospital	60	6541 (23.4)	8446 (30.2)	2456 (8.8)	289 (1.0)	10209 (36.5)	27941
Abidha Health Centre	36	979 (18.9)	1198 (23.1)	730 (14.1)	13 (0.3)	2270 (43.7)	5190
Madiany Health Centre	36	1808 (19.7)	1948 (21.2)	1171 (12.8)	53 (0.6)	4199 (45.7)	9179
Nyagoko Dispensary	36	539 (10.0)	1111 (20.7)	978 (18.2)	22 (0.4)	2717 (50.6)	5367
Gobei Dispensary	36	1383 (17.9)	2063 (26.7)	1116 (14.4)	48 (0.6)	3126 (40.4)	7736
Ujawi Dispensary	30	741 (10.9)	957 (14.1)	989 (14.6)	15 (0.2)	4082 (60.2)	6784
Overall 6 HFs		11991 **(19.3)**	15723 **(25.3)**	7440 **(12.0)**	440 **(0.7)**	26603 **(42.8)**	62197

[a] Total number of months between 1996 and 2001 for which data were collected
NS = children below 5 yrs without specified age; **HF** = health facility

2.3.1.4 *P. falciparum* prevalence rates

As previously mentioned, Bondo district is characterised by intense, perennial malaria transmission. The combined *P. falciparum* prevalence rate, among children aged 0-10 years, derived from 7 community-based surveys between 1959 and 1996 (Table 2.2), was 71.3% (range 47.9-88.5%). The combined prevalence rate in children less than one year was 60.8% (range 30.4-80.0%). Based on these data the district can be best described as hyper-holoendemic (Metselaar & Van Thiel, 1959).

Table 2.2: *P. falciparum* prevalence rates during the community surveys among children population in Bondo district, 1959 – 1996

Reference	M	< 1 year		1-4 years		5-10 years		All age (0-10 yrs)	
		Examined (positive)	PR (%)	Examined (positive)	PR (%)	Examined (positive)	PR (%)	Examined (positive)	PR (%)
Heisch, 1959	5	23 (7)	30.4	69 (54)	78.3	77 (36)	46.8	169 (97)	**57.4**
Anonymous, 1979	5	14 (8)	57.1	49 (37)	75.5	100 (70)	70.0	163 (115)	**70.6**
Anonymous, 1979	5	12 (5)	41.7	47 (40)	85.1	106 (34)	32.1	165 (79)	**47.9**
Kaseje, 1989	3	145 (77)	53.1	758 (517)	68.2	1256 (911)	72.5	2159(1505)	**69.7**
Kaseje, 1989	5	59 (47)	79.7	527 (469)	89.0	1200(1064)	88.7	1786(1580)	**88.5**
Ouma, 1994	2	10 (8)	80.0	35 (21)	60.0	428 (218)	50.9	473 (247)	**52.2**
Ouma, 1996	2	48 (37)	77.1	69 (48)	69.6	473 (218)	46.1	590 (303)	**51.4**

M = month in a year: 1 = January,...12 = December; **PR** = prevalence rate

2.3.1.5 Antimalarial drug resistance studies

In 2000 and 2003, EANMAT carried out two antimalarial drug sensitivity studies among children 6-59 months following the WHO protocols (WHO, 1996b; 2003d). The results showed that in studies over 14 days follow up the efficacy of SP was 66.7% in 2000 and 62.5% in 2003. During the study in 2003 the follow up was extended by day 28 and SP was efficacious in only 30.9% of children. During the same studies amodiaquine remained highly efficacious, however, in the most recent study with extended follow up over 28 days the efficacy was reduced to 83.0%. The results of antimalarial drug resistance studies in Bondo district are presented in Table 2.3.

Table 2.3: SP and amodiaquine drug resistance studies performed in Bondo district

Author	Drug	Year	Follow up completed	% ETF + LTF	% ACR-d14	% LPF	% ACPR-d14	% ACPR-d28[a]
EANMAT	SP	2000	60	26.7	73.3	6.7	66.7	ND
EANMAT	SP	2003	112	21.4	78.6	16.1	62.5	30.9
EANMAT	AQ	2000	59	0.0	100.0	0.0	100.0	ND
EANMAT	AQ	2003	114	0.9	99.1	0.9	98.2	83.0

[a] Results not PCR corrected for the possibility of reinfection

ETF (Early treatment failure) = development of danger signs or severe malaria within the first three days (with parasitaemia) or a history of fever (axillary temperature ≥37.5°C) on Day 2 or 3 in the presence of parasitaemia. Parasitaemia on Day 3 ≥25% of the count on Day 0 on its own also qualifies as ETF (WHO, 1996b); **LTF** (Late treatment failure) = recorded if danger signs or severe malaria occur on Days 4 to 14 (with parasitaemia), or there is fever with parasitaemia on Days 4 to 14 without previously meeting criteria for ETF (WHO, 1996b); **ACR** (Adequate clinical response) = achieved if there is no parasitaemia or no fever on Day 14 without previously meeting the criteria for ETF or LTF (WHO, 1996b); **LPF** (Late Parasitological Failure) = presence of parasitaemia on Day 14 or 28 and axillary temperature < 37.5°C, without previously meeting criteria for ETF or LTF (WHO, 2003d); **ACPR** (Adequate Clinical and Parasitological Response) = absence of parasitaemia on Day 14 (or Day 28), irrespective of axillary temperature, without previously meeting any of the criteria for ETF, LTF or LPF (WHO, 2003d); **ND** = not done

2.3.2 Kisii Central & Gucha Districts

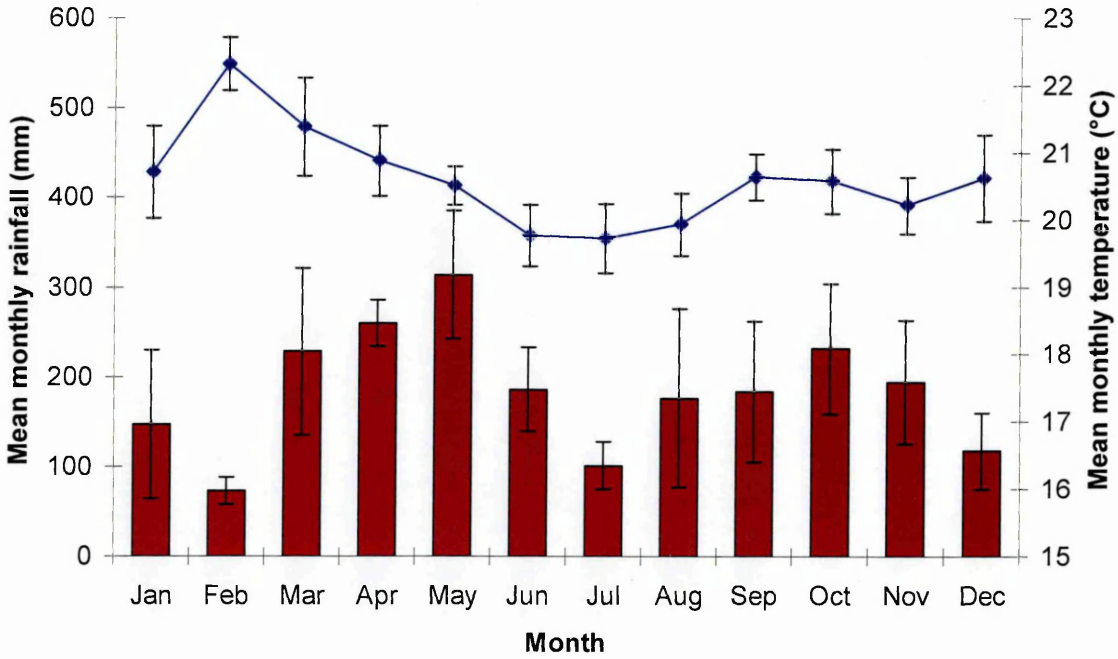
Former Kisii district was split in 1997 to form Kisii Central and Gucha districts. For the purpose of this study they will be regarded as Kisii district. The district is located in the southern highlands of Nyanza province and lies between latitude 0.5^0 and 0.967^0 south

and longitude 34.7^0 and 35.083^0 east. It occupies an area of about 1,310 km^2. According to the 1999 national census, the districts had a combined population of 952,725 people resulting in a population density of 727 persons per km^2 (CBS, 2001). The population are predominantly Kigusii. Nyanza Province infant and childhood mortality was 135 and 199 per 1000 live births respectively in 1998 (NCPD, 1999). The nutritional survey undertaken in Kisii district in 1994 among 261 children aged 6-59 months showed that 40.6% of children were stunted, 6.2% wasted and 23.4% were undernourished (CBS, 1994).

2.3.2.1 Climate characteristics

Kisii district is a hilly area located between 1200 and 2200 metres above sea level receiving an average of over 2000 mm of rainfall per year. Daily data on rainfalls and temperature were collected from Kisii Meteorological Station for the time period between 1998 and 2003. The monthly variations in the level of rainfall and temperature were expressed as the monthly means for the period 1998-2003 and presented in Figure 2.4. The total annual rainfall ranged from 2107 to 2305 mm/year with a monthly range of 31 to 424 mm of rain. The rainfall pattern is bimodal: long rains occur from March to June while the short rains occur from October to November. In the period 1998-2003, the average monthly maximum temperature was 25.8°C with a mean monthly range of 24.5-28.1°C, and the average monthly minimum temperature was 15.4°C with a mean monthly range of 14.6-16.5°C. The hottest month of the year is February just before the long rains while the coolest months are June and July at the end of the long rains (Figure 2.4.).

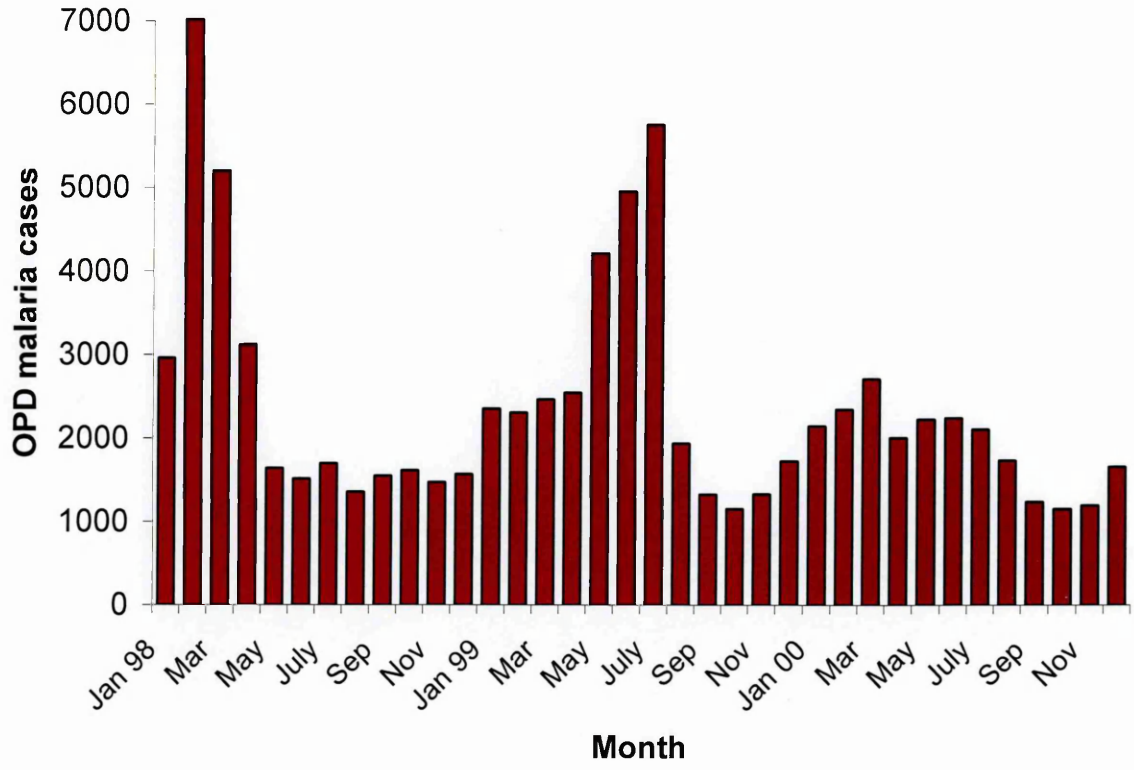
Figure 2.4: Mean monthly rainfall (bars) and mean monthly temperature (line) with intervals presenting one standard deviation around the monthly means: data from Kisii Meteorological Station, Kisii district, 1998-2003



2.3.2.2 Seasonality of malaria transmission

Malaria transmission is present throughout the year but is highly seasonal and varies in magnitude between years depending largely on rainfall and constitutes the typology of "highland" malaria (Cox *et al.*, 1999). The increase in malaria cases usually starts one month after the beginning of the rainy season and most frequently occurs between May and July and between January and March. In Kisii district, the paediatric, and older children and adult surveys were conducted in the months of July and March-April, respectively. The example of a consecutive series of monthly, outpatient, all age malaria diagnoses reported from Kisii District Hospital between January 1998 and December 2000 demonstrates the pattern of malaria seasons in the district (Figure 2.5.).

Figure 2.5: Consecutive series of monthly, outpatient, all age malaria diagnoses, Kisii District Hospital, January 1998 - December 2000



2.3.2.3 Age structured profile of outpatient malaria diagnoses

The age structured, monthly, outpatient malaria diagnoses were collected from 7 health facilities in Kisii district between 1998-2000 (Table 2.4). The age-specific distribution of malaria diagnoses shows that 9.6% (range 4.4-12.4%) of malaria diagnoses were reported in children less than one year, 20.0% (range 18.0-23.8%) in age group 1-4 years, and 20.9% (range 14.6-24.8%) in age group 5-14 years. Patients older than 14 years accounted for 48.8% (range 43.2-60.2%) of malaria diagnoses.

Table 2.4: Distribution of malaria diagnoses across age groups: results from 7 health facilities in Kisii district between 1998 and 2000

	No of months[a]	< 1 year (% total)	1-4 yrs (% total)	5-14 yrs (% total)	<5 yrs NS (% total)	≥ 15 yrs (% total)	Total
Keumbu Sub-D. Hospital	36	3308 (12.0)	4992 (18.1)	6856 (24.8)	519 (1.9)	11942 (43.2)	27617
Magena Dispensary	36	1389 (7.1)	4170 (21.2)	4640 (23.6)	0	9477 (48.2)	19676
Kenyenya Health Centre	23	747 (6.8)	2217 (20.2)	2193 (19.9)	29 (0.3)	5814 (52.9)	11000
Nyakwana Dispensary	20	596 (10.8)	1218 (22.0)	1131 (20.5)	39 (0.7)	2544 (46.0)	5528
Kisii District Hospital	7	1395 (9.1)	2927 (19.0)	2395 (15.5)	0	8697 (56.4)	15414
Gucha Sub-D. Hospital	8	1120 (12.4)	2147 (23.8)	1320 (14.6)	0	4450 (49.2)	9037
Magenche Dispensary	8	73 (4.4)	296 (18.0)	286 (17.4)	0	991 (60.2)	1646
Overall 7 HFs		8628 **(9.6)**	17967 **(20.0)**	18821 **(20.9)**	587 **(0.7)**	43915 **(48.8)**	89918

[a] Total number of months between 1998 and 2000 for which data were collected
NS = children below 5 yrs without specified age; **HF** = health facility

2.3.2.4 *P. falciparum* prevalence rates

The combined *P. falciparum* prevalence rate, among children aged 0-10 years, derived from 8 community-based surveys between 1994 and 2000 (Table 2.5), was 26.0% (range 10.9-70.7%). The combined prevalence rate in children less than one year was 15.7% (range 0-53.6%). Based on the prevalence rate the district can be best described as mesoendemic (Metselaar & Van Thiel, 1959).

Table 2.5: *P. falciparum* prevalence rates during the community surveys among children population in Kisii district in 1994 and 2000

Reference	M	< 1 year		1-4 years		5-10 years		All age (0-10 yrs)	
		Examined (positive)	PR (%)	Examined (positive)	PR (%)	Examined (positive)	PR (%)	Examined (positive)	PR (%)
UNICEF, 1994	4	28 (15)	53.6	232 (166)	71.6	54 (41)	75.9	314 (222)	**70.7**
UNICEF, 1994	4	33 (17)	51.5	203 (139)	68.5	51 (29)	56.9	287 (185)	**64.5**
Zurovac, 2000	3	10 (0)	0	60 (4)	6.7	160 (21)	13.1	230 (25)	**10.9**
Zurovac, 2000	3	20 (1)	5.0	42 (9)	21.4	126 (26)	20.6	188 (36)	**19.1**
Zurovac. 2000	4	15 (0)	0	67 (8)	11.9	183 (30)	16.4	265 (38)	**14.3**
Zurovac, 2000	4	20 (0)	0	81 (13)	16.1	190 (42)	22.1	291 (55)	**18.9**
Zurovac, 2000	5	41 (0)	0	217 (29)	13.4	547 (89)	16.3	805 (118)	**14.7**
Zurovac, 2000	5	56 (2)	3.6	187 (27)	14.4	387 (76)	19.6	630 (105)	**16.7**

M = month in a year: 1 = January,...12 = December; **PR** = prevalence rate

2.3.2.5 Antimalarial drug resistance studies

The recent results of antimalarial drug sensitivity studies according to the WHO protocol (WHO, 1996b; 2003d) show that efficacy of SP and amodiaquine over 14 day follow up was 70.4% and 94.7% respectively. However, extended follow up over 28 days demonstrated low success rates for both drugs: amodiaquine efficacy declined to 77.0% and the efficacy of SP was only 39.6%. The results of antimalarial drug resistance studies are presented in Table 2.6.

Table 2.6: SP and amodiaquine drug resistance studies performed in Kisii district[a]

Author	Drug	Year	Follow up completed	% ETF + LTF	% ACR-d14	% LPF	% ACPR-d14	% ACPR-d28[b]
EANMAT	SP	2003	108	29.6	70.4	0.0	70.4	39.6
EANMAT	AQ	2003	131	5.3	94.7	0.0	94.7	77.0

[a] Definitions of treatment outcomes are provided under Table 2.3
[b] Results not PCR corrected for the possibility of reinfection

2.3.3. Kwale district

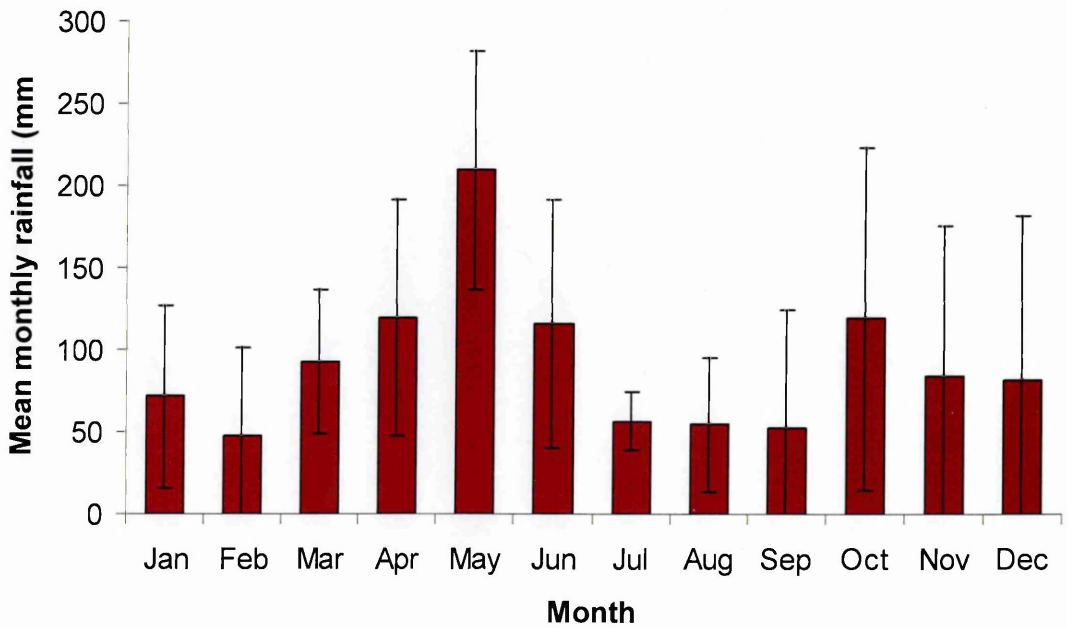
Kwale district is one of the seven districts in Coast province, located in the south-eastern corner of Kenya on the border with Tanzania. The district lies between latitudes 3.55° south and 4.667° south and longitudes 38.45° and 39.667° east. Kwale district is located along the Indian Ocean on the east and the United Republic of Tanzania to the south. According to the 1999 national population census the district had a population of 496,133 (CBS, 2001). The district has a land surface of 8,335 km^2 and low population density of 60 persons per km^2. The majority of the population are of the Mijikenda ethnic group (80%). The Coast province has infant and childhood mortality of 70 and 96 per 1000 live births respectively (NCPD, 1999). The nutritional survey undertaken in Kwale district in

1994 among children aged 6-59 months showed that 53.0% of the children were stunted, 5.2% were wasted and 29.1% were undernourished (CBS, 1994).

2.3.3.1 Climate characteristics

Daily data on rainfall were collected from Kinango Agricultural Institute for the time period between 1998 and 2003. Data on temperatures were not available. The total annual rainfall ranged from 711 to 1353 mm/year with a range of 0 to 310 mm of rain a month. The long rains usually occur between March and June. The short rains occur most commonly between October and January, however with significant variations between the years. The monthly variations in the level of rainfalls were expressed as the monthly mean for the period 1998-2003 and presented in Figure 2.6.

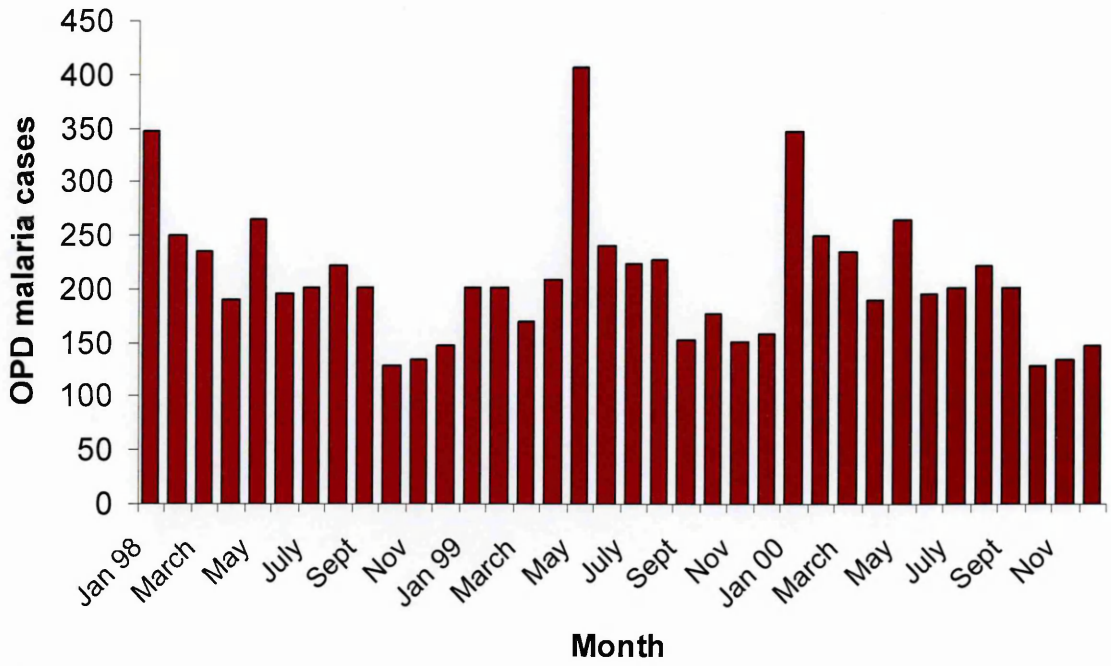
Figure 2.6: Mean monthly rainfall with intervals presenting one standard deviation around the monthly means: data from Kinango Agricultural Institute, Kwale district, 1998-2003



2.3.3.2 Seasonality of malaria transmission

Malaria transmission in Kwale is stable, present throughout the year, with seasonal distribution associated with rainfall patterns. The increase in malaria cases usually occurs between May and September, and between January and February. The paediatric, and older children and adult surveys were conducted in the months of August, and August-September, respectively. The example of a consecutive series of monthly, outpatient, all age malaria diagnoses reported from Mackinon Dispensary between January 1998 and December 2000 demonstrates the pattern of malaria seasons in the district (Figure 2.7.).

Figure 2.7: Consecutive series of monthly, outpatient, all age malaria diagnoses, Mackinon Dispensary, January 1998 - December 2000



2.3.3.3 Age structured profile of outpatient malaria diagnoses

The age structured, monthly, outpatient malaria diagnoses were collected from 5 health facilities in Kwale district between 1998 and 2000 (Table 2.7). The age-specific

distribution of malaria diagnoses shows that 12.8% (range 4.4-14.8%) of malaria diagnoses were reported in children less than one year, 24.0% (range 20.0-30.7%) in the age group 1-4 years, and 15.6% (range 12.3-18.4%) in the age group 5-14 years. Patients older than 14 years accounted for 46.9% (range 43.1-58.1%) of malaria diagnoses.

Table 2.7: Distribution of malaria diagnoses across age groups, results from 5 health facilities in Kwale district between 1998 and 2000

	No of months[a]	< 1 year (% total)	1-4 yrs (% total)	5-14 yrs (% total)	<5 yrs NS (% total)	≥ 15 yrs (% total)	Total
Mackinon Dispensary	36	387 (4.4)	1787 (20.5)	1471 (16.8)	16 (0.2)	5075 (58.1)	8736
Lunga Lunga Dispensary	36	2429 (14.4)	3363 (20.0)	2955 (17.5)	90 (0.5)	8005 (47.5)	16842
Vigurangani Dispensary	36	1295 (14.8)	2004 (22.9)	1608 (18.4)	2 (0.02)	3829 (43.8)	8738
Kikoneni Health Centre	35	1806 (13.1)	4241 (30.7)	1700 (12.3)	116 (0.8)	5947 (43.1)	13810
Msambweni District Hospital	24	1280 (16.2)	2029 (25.7)	1033 (13.1)	134 (1.7)	3431 (43.4)	7907
Overall 5 HFs		7197 **(12.8)**	13424 **(24.0)**	8767 **(15.6)**	358 **(0.6)**	26287 **(46.9)**	56033

[a] Total number of months between 1998 and 2000 for which data were collected
NS = children below 5 yrs without specified age; **HF** = health facility

2.3.3.4 *P. falciparum* prevalence rates

The combined *P. falciparum* prevalence rate, among children aged 0-10 years, derived from 8 community-based surveys between 1968 and 2003, has shown to be 61.3% (range 31.0-87.0%). The combined parasite rate in children less than one year has shown to be 49.5% (range 26.7-68.6%). Based on the prevalence rate the district can be best described as hyperendemic (Metselaar & Van Thiel, 1959).

Table 2.8: *P. falciparum* prevalence rates during the community surveys among children population in Kwale district, 1968 – 2003

Reference	M	< 1 year		1-4 yrs		5-10 yrs		All age (0-10 yrs)	
		Examined (positive)	PR (%)	Examined (positive)	PR (%)	Examined (positive)	PR (%)	Examined (positive)	PR (%)
Obwond, 1968	4	15 (4)	26.7	130(45)	34.6	65 (16)	24.6	210 (65)	**31.0**
Anonymous, 1979	11	18 (6)	33.3	30(14)	46.7	95 (27)	28.4	143 (47)	**32.9**
Anonymous, 1979	11	15 (7)	46.7	24(12)	50.0	190 (152)	80.0	229 (171)	**74.7**
Lugogo, 1994	3	0	NA	50(23)	46.0	84 (28)	33.3	134 (51)	**38.1**
Marsh, 2003	8	31 (20)	64.5	216(195)	90.3	ND	NA	247 (215)	**87.0**
Marsh, 2003	8	44 (21)	47.7	210(119)	56.7	ND	NA	254 (140)	**55.1**
Marsh, 2003	8	42 (17)	40.5	200(147)	73.5	ND	NA	242 (164)	**67.8**
Marsh, 2003	8	35 (24)	68.6	185(152)	82.2	ND	NA	220 (176)	**80.0**

M = month in a year: 1=January,...12=December; **PR** = prevalence rate; **ND** = not done; **NA** = not applicable

2.3.3.5 Antimalarial drug resistance studies

In 2000 and 2001, EANMAT carried out two antimalarial drug sensitivity studies among children 6-59 months following the WHO protocol with follow up over 14 days (WHO 1996b). The results showed that efficacy of SP declined from 96.8% in 2000 to 86.8% in 2001. In the same studies, amodiaquine remained highly efficacious, with low rates of treatment failures ranging from 0 to 2.5%. Until now, the studies with follow up over 28 days were not performed in Kwale district. The results of antimalarial drug resistance studies undertaken in Kwale district are presented in Table 2.9.

Table 2.9: SP and amodiaquine drug resistance studies performed in Kwale district[a]

Author	Drug	Year	Follow up completed	% ETF + LTF	% ACR-d14	% LPF	% ACPR-d14	% ACPR-d28
EANMAT	SP	2000	63	0.0	100.0	3.2	96.8	ND
EANMAT	SP	2001	53	7.6	92.4	5.7	86.8	ND
EANMAT	AQ	2000	64	0.0	100.0	1.6	98.4	ND
EANMAT	AQ	2001	57	0.0	100.0	0.0	100.0	ND

[a] Definitions of treatment outcomes are provided under Table 2.3; **ND** = not done

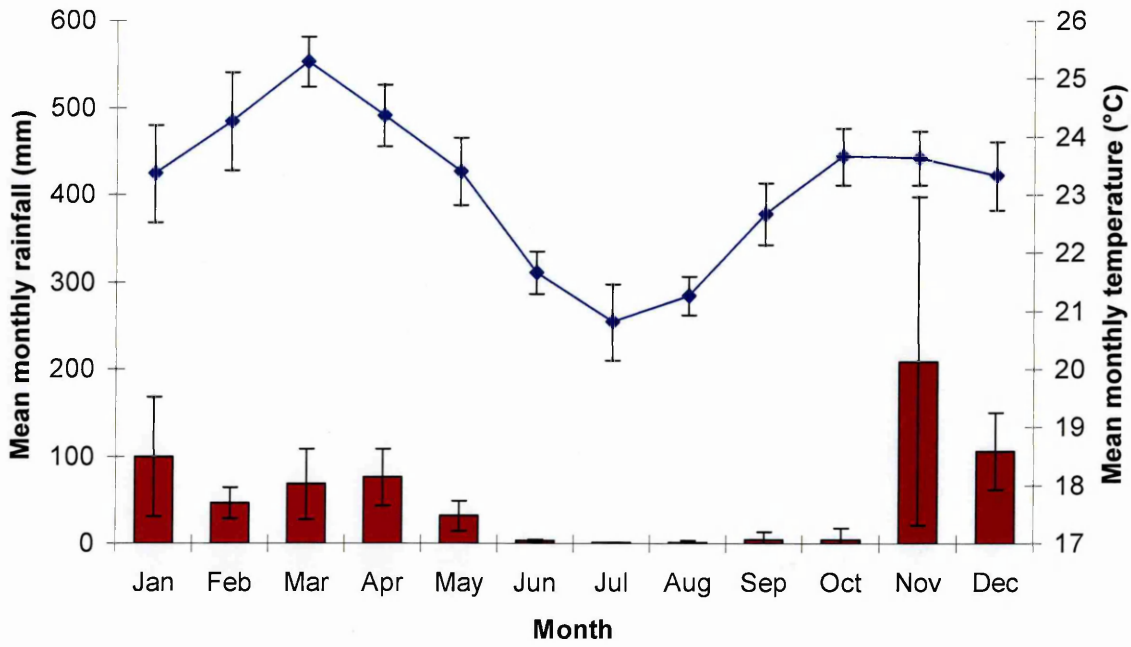
2.3.4 Makueni district

Makueni district is one of the twelve districts of Eastern Province and lies between longitudes 37.144° and 38.517° east and latitudes 1.523° and 2.987° south and covers a land surface area of 8,266 km². According to the 1999 population census, the district had a population 771,545 people with an average density of 97 persons per km^2 (CBS, 2001). The majority of the population are WaKamba (97%). The Eastern province has infant and childhood mortality of 53 and 77 per 1000 live births respectively (NCPD, 1999). The nutritional survey undertaken in Makueni district in 1994 among children aged 6-59 months showed that 50.0% of the children were stunted, 2.7% were wasted and 22.3% were undernourished (CBS, 1994).

2.3.4.1 Climate characteristics

Daily data on rainfall and temperature were collected from Makindu Meteorological Station for the time period between 1998 and 2003. The monthly variations in the level of rainfall and temperature were expressed as the monthly means for the period 1998-2003 and presented in Figure 2.8. The total annual rainfall ranged from 521 to 1003 mm/year with a monthly range of 0 to 537 mm of rain. The long rains occur mainly between March and April with short rains between November and January. The time period between June and October is usually dry with very little rainfall. In the period 1998-2003, the average monthly maximum temperature was 28.9°C with a mean monthly range of 26.8-31.2°C, and the average monthly minimum temperature was 17.3°C with a mean monthly range 14.7-19.3°C. The hottest month of the year is March at the beginning of the long rains while the coolest months are June to August after the long rain season (Figure 2.8.).

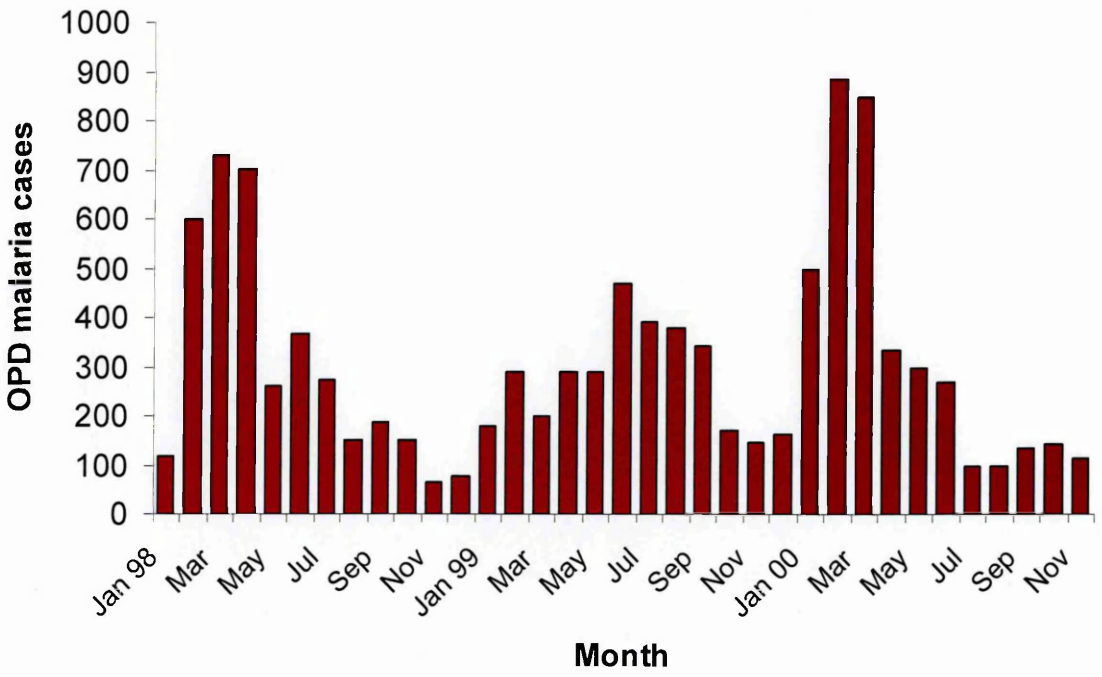
Figure 2.8: Mean monthly rainfall (bars) and mean monthly temperature (line) with intervals presenting one standard deviation around the monthly means: data from Makindu Meteorological Station, Makueni district, 1998-2003



2.3.4.2 Seasonality of malaria transmission

Malaria transmission is acutely seasonal and largely dependent on the level of rainfall. The increase in malaria cases starts after the beginning of the rainy season and usually occurs between January and March and between June and July. The paediatric survey in Makueni district was conducted in the month of February. The example of a consecutive series of monthly, outpatient, all age malaria diagnoses reported from Kato Dispensary between January 1998 and December 2000 demonstrates the pattern of malaria seasons in the district (Figure 2.9.).

Figure 2.9: Consecutive series of monthly, outpatient all age malaria diagnoses, Kato Dispensary, January 1998 - December 2000



2.3.4.3 Age structured profile of outpatient malaria diagnoses

The age structured, monthly, outpatient malaria diagnoses were collected from 5 health facilities in Makueni district between 1998 and 2000 (Table 2.10). The age-specific distribution of malaria diagnoses shows that 7.3% (range 5.3-11.4%) of malaria diagnoses were reported in children less than one year, 16.0% (range 12.8-21.1%) in the age group 1-4 years, and 28.4% (range 19.5-32.8%) in the age group 5-14 years. Patients older than 14 years accounted for 45.1% (range 39.8-48.9%) of malaria diagnoses.

Table 2.10: Distribution of malaria diagnoses across age groups, results from 5 health facilities in Makueni district between 1998 and 2000

	No of months[a]	< 1 year (% total)	1-4 yrs (% total)	5-14 yrs (% total)	<5 yrs NS (% total)	≥ 15 yrs (% total)	Total
Kato Dispensary	35	633 (5.9)	1677 (15.6)	3525 (32.8)	274 (2.5)	4617 (42.9)	10761
Kathonzweni Dispensary	35	718 (5.3)	1784 (13.2)	3986 (29.4)	410 (3.0)	6656 (40.2)	13554
Nzui Dispensary	36	1327 (11.4)	2136 (18.3)	3182 (27.3)	372 (3.2)	4641 (39.8)	11658
Kikumini Health Centre	24	220 (6.2)	454 (12.8)	1025 (28.9)	155 (4.4)	1696 (47.8)	3550
Sultan Hamud Health Centre	24	369 (6.7)	1168 (21.1)	1080 (19.5)	210 (3.8)	2709 (48.9)	5536
Overall 5 HFs		3267 **(7.3)**	7219 **(16.0)**	12798 **(28.4)**	1421 **(3.2)**	20319 **(45.1)**	45024

[a] Total number of months between 1998 and 2000 for which data were collected
NS = children below 5 yrs without specified age; **HF** = health facility

2.3.4.4 *P. falciparum* prevalence rates

Characteristic of the district is acute seasonal low intensity malaria transmission with marked spatial heterogeneity. The combined *P. falciparum* prevalence rate, among children aged 0-10 years, derived from 7 community-based surveys between 1951 and 2003 (Table 2.11), has shown to be 11.5% (range 0.4-33.3%). The combined parasite rate in children less than one year was 6.2% (range 0-28.9%). Based on the prevalence rate the district can be best described as hypo-mesoendemic (Metselaar & Van Thiel, 1959).

Table 2.11: *P. falciparum* prevalence rates during the community surveys among children population in Makueni district

Reference	M[a]	< 1 year		1-4 yrs		5-10 yrs		All age (0-10 yrs)	
		Examined (positive)	PR (%)	Examined (positive)	PR (%)	Examined (positive)	PR (%)	Examined (positive)	PR (%)
CPK, 1951	NR	38 (5)	13.2	61 (16)	26.2	118 (21)	17.8	217 (42)	**19.4**
CPK, 1951	NR	38 (11)	28.9	61 (19)	31.1	118 (21)	17.8	217 (51)	**23.5**
Mugo, 1993	8	0	NA	57 (18)	31.6	102 (35)	34.3	159 (53)	**33.3**
Marsh, 2003	8	52 (0)	0	214 (7)	3.3	ND	NA	266 (7)	**2.6**
Marsh, 2003	8	49 (0)	0	189 (1)	0.5	ND	NA	238 (1)	**0.4**
Marsh, 2003	8	52 (0)	0	173 (8)	4.6	ND	NA	225 (8)	**3.6**
Marsh, 2003	8	44 (1)	2.3	204 (17)	8.3	ND	NA	248 (18)	**7.3**

M = month in a year: 1 = January,...12 = December; **PR** = prevalence rate; **ND** = not done; **NA** = not applicable

2.3.4.5 Antimalarial drug resistance studies

The results of antimalarial drug sensitivity studies with follow up over 14 days (WHO, 1996b) showed that efficacy of SP declined from 81.8% in 2000 to 45.2% in 2002. The most recent study carried out by EANMAT reported that efficacy of SP over 14 days follow up was 83.1%; however, the same study revealed that SP was efficacious in only 46.4% of children with extended follow up over 28 days (WHO, 2003d). Between 2000 and 2003, four studies with follow up over 14 days, reported efficacy of amodiaquine to be in range 84.0-100%; however, the most recent study in 2003 with extended follow up over 28 days revealed that the efficacy of amodiaquine declined to 68.5%. The results of antimalarial drug resistance studies are presented in Table 2.12.

Table 2.12: SP and amodiaquine drug resistance studies performed in Makueni district [a]

Author	Drug	Year	Follow up completed	% ETF + LTF	% ACR-d14	% LPF	% ACPR-d14	% ACPR-d28 [b]
EANMAT	SP	2000	11	18.2	81.8	0.0	81.8	ND
EANMAT	SP	2001	19	15.8	84.2	10.5	73.7	ND
EANMAT	SP	2002	31	51.6	48.4	3.2	45.2	ND
EANMAT	SP	2003	71	8.5	91.6	8.5	83.1	46.4
EANMAT	AQ	2000	14	7.1	92.9	0.0	92.9	ND
EANMAT	AQ	2001	25	16.0	84.0	0.0	84.0	ND
EANMAT	AQ	2002	34	0.0	100.0	0.0	100.0	ND
EANMAT	AQ	2003	95	8.4	91.6	3.2	88.4	68.5

[a] Definitions of treatment outcomes are provided under Table 2.3;
[b] Results not PCR corrected for the possibility of reinfection; **ND** = not done

2.3.5 Summary characteristics of four study districts

The major characteristics of four study districts related to their population, climate, malariology, antimalarial drug efficacy studies and timing of the surveys are summarised in Table 2.13

Table 2.13: Summary characteristics of four study districts

Characteristics	BONDO	KISII	KWALE	MAKUENI
Population	238,780	952,725	496,133	771,545
Density of population per km^2	242	727	60	97
Climate				
Long rain season[a]	Mar-May	Mar-June	Mar-June	Mar-April
Short rain season[a]	Sep-Jan	Oct-Nov	Oct-Jan	Nov-Jan
Hottest month	February	February	NA	March
Coolest month	June	July	NA	July
Malariology				
P.falciparum PRs (range)	71.3% (47.9-88.5%)	26.0% (10.9-70.7%)	61.3% (31.0-87.0%)	11.5% (0.4-33.3%)
Endemicity classification	Hyper-holoendemic	Mesoendemic	Hyperendemic	Hypo-mesoendemic
Malaria seasons[a]	May-July Dec-Feb	Jan-Mar May-July	Jan-Feb May-Sep	Jan-Mar June-July
Age-profile of malaria diagnoses				
<5 years (%)	45.3	30.3	37.4	26.5
5-14 years (%)	12.0	20.9	15.6	28.4
>14 years (%)	42.8	48.8	46.9	45.1
Antimalarial drug efficacy (latest studies)				
SP (ACPR-d14)	62.5	70.4	86.8	83.1
SP (ACPR-d28)	30.9	39.6	ND	46.4
Amodiaquine (ACPR-d14)	98.2	77.0	100	88.4
Amodiaquine (ACPR-d28)	83.0	94.7	ND	68.5
Time of studies				
Children survey	Oct 2001	July 2001	Aug 2001	Feb 2002
Older children and adult survey	ND	Mar-Apr 2003	Aug-Sep 2003	ND

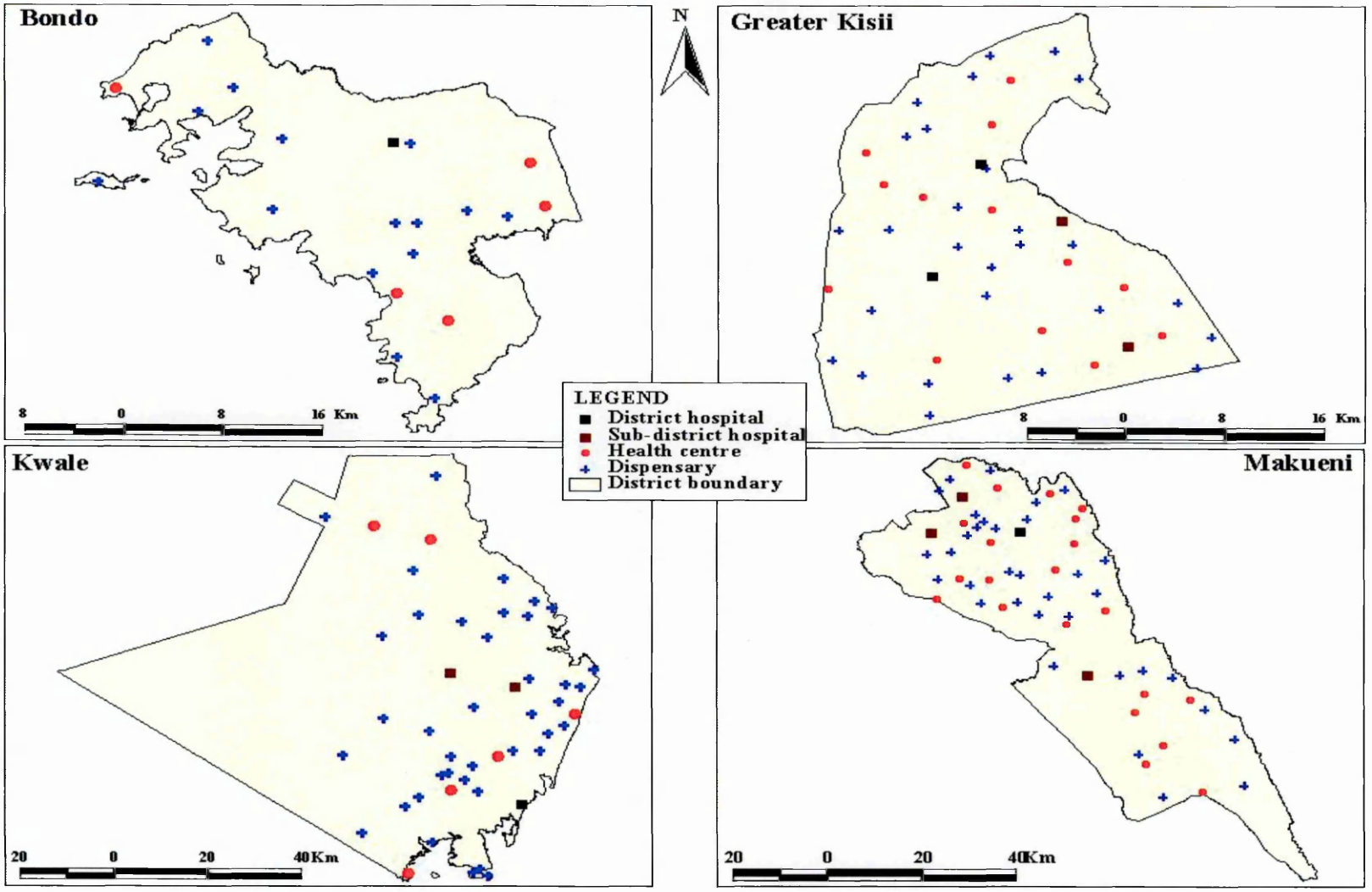
[a] Seasons usually occur between these months but may vary between years
PR = prevalence rate; **ND** = not done; **NA** = not available; **ACPR** = Adequate Clinical and Parasitological Response

2.4 Development of district Geographic Information System maps

To develop health facility sampling frames and facilitate effective planning of the survey, a spatially linked database of health facilities was developed for each of four districts. These health facility databases were based on the provisional district specific lists, reports and maps found in Nairobi at the Ministry of Health, Christian Health Association of Kenya, Family Planning Logistic Management Organisation, Central Bureau of Statistics and the Government's Gazette. Furthermore, the existence of each facility was

counterchecked with District Health Management Teams (DHMT) and the lists were updated where necessary. Finally each facility was visited and a precise longitude and latitude was taken using a hand-held Global Positioning System (GPS). During the facility visit, basic information was also collected on the type and ownership of facility, staffing characteristics and type of services provided. The positions of all health facilities were then overlaid into the previously digitised district maps encompassing administrative boundaries, transport networks, rivers and other water bodies among other features (Noor *et al.,* 2003). This thesis focuses on Government of Kenya (GoK) health facilities. The study district maps displaying the GPS positioned GoK health facilities according to the facility type are presented in Figure 2.10.

Figure 2.10: Study district maps with GPS positioned government health facilities



2.5 Government health service structure with respect to malaria case management

In Kenya, at the level of district, the provision of government health services is primarily organised through a three-tiered health system comprising dispensaries, health centres and a district hospital. With respect to malaria case management, dispensaries provide only outpatient care, without laboratory support and are supposed to stock nationally recommended, first (oral SP), second-line (oral amodiaquine or quinine) and pre-referral (injectable quinine) antimalarial drugs. Health centres provide outpatient and limited 24-hour inpatient care, have laboratory support and are supposed to stock first and second-line outpatient drugs and drugs for the management of severe malaria; there are no blood transfusion services available. A district hospital provides outpatient and inpatient care including blood transfusion services, has laboratory support, and should stock all drugs and equipment necessary for the management of uncomplicated and severe malaria. A small number of sub-health centres and sub-district hospitals, as the inter-level health facilities, also exist. Since the service capacities of these levels of care, related to malaria case management, do not differ significantly from any of the above belonging to the three-tiered structure, for the purpose of this study, sub-health centres can be classified with dispensaries and sub-district hospitals with health centres. Nurses and clinical officers provide outpatient services in dispensaries and district hospitals respectively. In health centres, outpatient consultations are performed by both nurses and clinical officers. The distribution of GoK health facilities across four districts and type of health facility is shown in Table 2.14.

Table 2.14: Distribution of government health facilities across districts and types of facility

Type of health facility	BONDO	KISII	KWALE	MAKUENI	TOTAL
Dispensary	15	27	39	34	115
Sub-health centre	0	3	0	10	13
Health centre	5	10	6	11	32
Sub-district hospital	0	3	2	3	8
District hospital	1	1	1	1	4
All facilities	21	44	48	59	172

2.6 Development of the final sampling frame

2.6.1 Development of the final sampling frame for the paediatric survey

The sampling frame for the paediatric survey was stratified by the type of health facility. Health facilities considered not relevant for our survey by either not providing general outpatient services, not operating regularly or not functional during the survey days were excluded from the sampling frame. Two strata of health facilities providing outpatient care were defined: 1) dispensaries, and 2) combined health centres and district hospitals (each district had only one district hospital).

The primary units of analysis for this survey were sick child consultations; therefore, to maximise recruitment of patients and optimise the use of limited resources, facilities attending too few sick children in a day (defined as less than five on average) were excluded from the sampling frame. The exclusion of facilities using patients' caseload was based on the monthly attendance figures from the same month of the previous year. These figures were obtained through routine health facility morbidity reports and retrospective surveys collecting data on age-specific malaria burden for DOMC's monitoring and evaluation activities. For each facility an average number of children seen per day was calculated by dividing the monthly number of children by an average of 22

working days in a month. The health facilities were ordered according to the average daily paediatric (0-4 years) caseload. The monthly cumulative number and percentage of sick child consultations was attributed to each facility within each stratum.

By applying exclusion criterion of less than 5 sick children a day, cumulative percentage of excluded facilities was calculated with attributed cumulative percent of excluded sick child consultations for each stratum (dispensaries versus health centres and hospitals), district and for four districts together. None of the health centres and district hospitals were excluded from the sampling frame. Among dispensaries, the highest percentage of excluded facilities across four districts was in Kisii district (24.1%). The highest cumulative percentage of excluded sick child consultations among all dispensary strata was also in Kisii district (8.5%). Overall, among all types of facility in four districts, only 1.8% of potential sick child consultations were excluded from the sampling frame.

It was important that this procedure did not exclude too many facilities and sick child consultations from the universe of the sampling frame. The WHO recommends that if more than 25-30% of sick children are seen in excluded facilities, then the sample should include these facilities (WHO, 2002b). In this study, the WHO cut-off of 25% was not exceeded in any of the strata sampled. Table 2.15 shows development of the sampling frame for the paediatric survey and the percentage of excluded facilities and sick child consultations.

Table 2.15: Development of the sampling frame for paediatric survey

District	Sampling frame (GIS)[a]	Sampling frame (NR)[b]	Sampling frame (Final)[c]	Excluded facilities (%)[d]	Excluded children (%)[e]
KWALE					
Dispensaries	39	38	36	5.3	0.9
HC/DH	9	9	9	0	0
All facilities	48	47	45	4.3	0.5
KISII					
Dispensaries	30	29	22	24.1	8.5
HC/DH	14	14	14	0	0
All facilities	44	43	35	18.6	5.4
BONDO					
Dispensaries	15	13	12	7.7	1.3
HC/DH	6	5	5	0	0
All facilities	21	18	17	5.6	0.9
MAKUENI					
Dispensaries	44	40	37	7.5	1.7
HC/DH	15	15	15	0	0
All facilities	59	54	51	5.6	1.1
TOTAL					
Dispensaries	128	121	107	11.6	2.8
HC/DH	44	42	42	0	0
All facilities	172	163	149	8.6	1.8

[a] Initial GIS sampling frame (Table 2.14)
[b] Sampling frame after exclusion of non-relevant facilities
[c] Final sampling frame after excluding facilities seeing in average less than 5 sick children in a day
[d] Percentage of facilities excluded from the sampling frame adjusted for non-relevant facilities
[e] Cumulative percent of sick child consultations excluded from the sampling frame (NR)
HC = health centre; **DH** = district hospital; **NR** = non-relevant;

2.6.2 Development of the final sampling frame for the older children and adult survey

The older children and adult survey was undertaken in two districts (Kisii and Kwale) and the sampling frame was stratified in each district according to the availability of functional malaria microscopy at health facilities. Two strata were defined: 1) facilities without microscopy, and 2) facilities with microscopy.

To obtain the final sampling frame of health facilities for each district, the same patient caseload exclusion criteria as described previously for the paediatric survey was used and

the percentage of excluded facilities with attributed cumulative percent of excluded patients was calculated. The calculation was done for each stratum (facilities with and without microscopy), each district and for the two districts together. None of the facilities with microscopy were excluded from the sampling frame. Among facilities without microscopy the highest percent of excluded facilities (10.3%) and patients (8.5%) was in Kisii district. Among all facilities in both districts, 8.1% were excluded from the sampling frame. These facilities attended only 7.4% of all patients older than 5 years. More facilities and patients were excluded in Kwale (8.5% and 3.3% respectively) than in Kisii district (7.7% and 4.8% respectively). Table 2.16 shows development of the sampling frame for the older children and adult survey and percentage of excluded facilities and patients' consultations across two districts and two strata.

Table 2.16: Development of sampling frame for older children and adult survey

District	Sampling frame (GIS)[a]	Sampling frame (NR)[b]	Sampling frame (Final)[c]	Excluded facilities[e] (%)[d]	Excluded patients (%)[e]
KWALE					
HFs without microscopy	34	33	29	12.1	4.8
HFs with microscopy	14	14	14	0	0
All facilities	48	47	43	8.5	3.3
KISII					
HFs without microscopy	34	29	26	10.3	8.5
HFs with microscopy	10	10	10	0	0
All facilities	44	39	36	7.7	4.8
TOTAL					
HFs without microscopy	68	62	55	11.3	5.2
HFs with microscopy	24	24	24	0	0
All facilities	92	86	79	8.1	7.4

[a] Initial GIS sampling frame (Table 2.14)
[b] Sampling frame after exclusion of non-relevant (NR) facilities
[c] Final sampling frame after excluding facilities seeing in average less than 5 sick patients in a day
[d] Percentage of facilities excluded from the sampling frame adjusted for non-relevant facilities
[e] Cumulative percent of patients consultations excluded from the sampling frame (NR)
HF = health facility; **NR** = non-relevant

2.7 Sampling procedures

2.7.1 Sampling procedures for paediatric survey

The paediatric survey was a cross-sectional, stratified, cluster sample health facility survey. A cluster was defined as all health worker-sick child consultations occurring at a facility during two survey days. As explained in the section 2.6.1, in each district two strata were defined according to the type of health facility. Using the average daily sick child attendance figures it was estimated that a minimum 8-10 dispensaries and 7-8 health centres (depending on the district) should be surveyed over two days each to provide an estimated sample size of 200 health worker-sick child consultations in each stratum within a district. Between 10 and 12 working days (Monday-Friday) were allocated for the survey in each of the districts. For a survey of 10 working days with four survey teams visiting each facility over two days, a maximum number of 20 health facilities could be surveyed.

For each health facility type stratum the number of facilities to be surveyed was determined by the number of facilities required to obtain the estimated sample size of children and the number of available days allocated for the survey. Health facilities in each stratum were sampled by systematic random sampling (apart from purposive selection of a district hospital) if the number of facilities in the sampling frame exceeded the minimum number of facilities required. In the strata where the number of facilities in the sampling frame was equal or below the required number of facilities all health facilities were surveyed. To increase precision of estimates and account for uncertainty in the size of design effect, in the strata where the number of facilities in the sampling frame

and number of days allocated for the survey allowed greater number of facilities to be surveyed than required, the greater sample of health facilities was selected.

Systematic random sampling was applied by ordering the sampling frame of health facilities in each stratum according to the children caseload and defining the sampling interval by dividing the number of facilities in the sampling frame with the maximum number of facilities that could be sampled within the survey time period. The first selected facility was decided using the random number table and presented the starting point of the sample. The next facility from the list was selected by counting down for the sampling interval. The procedure was repeated until the maximum sample size of health facilities in each stratum was obtained. After all health facilities had been selected, they were randomly assigned to the consecutive pair of two working days (Monday to Friday) within the time period allocated for the survey in each district. Surveys were undertaken during malaria seasons according to the following schedule: Kisii - July 2001, Kwale – August 2001, Bondo – October 2001 and Makueni – February 2002. The sampling process for paediatric survey is presented in Table 2.17.

Table 2.17: Sampling process for paediatric survey across the districts and strata

District	Sampling frame	Average No of children per HF per 2 days	No of required facilities[b]	Max. No of HFs to be surveyed[c]	No of surveyed facilities	No of enrolled children
KWALE (12 days[a])						
Dispensaries	36	23	9	15	15	228
HC/DH	9	25	8	9	9	204
KISII (10 days[a])						
Dispensaries	22	25	8	10	10	208
HC/DH	14	32	7	10	9	267
BONDO (10 days[a])						
Dispensaries	12	22	9	12	12	218
HC/DH	5	30	7	5	5	175
MAKUENI (11 days[a])						
Dispensaries	37	20	10	11	11	173
HC/DH	15	26	8	11	10	221

[a] Number of working days (Monday-Friday) allocated for the survey
[b] Number of required facilities obtained by dividing estimated sample size (200) with average number of sick children per facility over two days
[c] Maximum number of facilities which could be surveyed given the number of available days for the survey and number of facilities in the sampling frame;
HF = health facility; **HC** = health centre; **DH** = district hospital

2.7.2 Sampling procedures for older children and adult survey

The older children and adult survey was a cross-sectional, stratified, cluster sample health facility survey conducted in two districts, Kwale and Kisii. As explained in Section 2.6.2, in each district two strata were defined according to the availability of functional malaria microscopy at the health facility. A cluster was defined as all consultations for patients above 5 years of age occurring at a facility during two survey days. Using the average daily attendance figures for outpatients above 5 years it was estimated that a minimum of 10 and 7 facilities in Kwale and Kisii respectively should be surveyed over two days each to provide an estimated sample size of 200 health worker-patient observations at facilities with microscopy. At facilities without microscopy, it was estimated that a minimum 15 and 14 facilities in Kwale and Kisii respectively should be surveyed over two days each to provide an estimated sample size of 400 health worker-patient observations. The

survey was carried out with one field team and 50 and 42 working days (Monday-Friday) were allocated for the surveys in Kwale and Kisii districts respectively.

Health facilities in each district and each stratum were sampled by systematic random sampling using the same sampling procedure as in the paediatric survey (Table 2.18). After all health facilities had been selected, they were randomly assigned to the consecutive pair of two working days (Monday to Friday) within the time period allocated for the survey in each district. Surveys were undertaken during the expected malaria seasons according to the following schedule: Kwale - August and September 2002 and Kisii – March and April 2003.

Table 2.18: Sampling process for older children and adult survey across districts and strata

District	Sampling frame	Average No of patients per HF per 2 days	No of required facilities[b]	Max. No of HFs to be surveyed[c]	No of surveyed facilities	No of enrolled patients
KWALE (50 days[a])						
HFs without microscopy	29	29	15	15	15	412
HFs with microscopy	14	33	7	10	10	218
KISII (42 days[a])						
HFs without microscopy	26	20	14	14	14	418
HFs with microscopy	10	29	7	7	7	210

[a] Number of working days (Monday-Friday) allocated for the survey
[b] Number of required facilities obtained by dividing estimated sample size (400 at HFs without microscopy and 200 at HFs with microscopy) with an average number of sick patients >5 years of age per facility over two days
[c] Maximum number of facilities which could be surveyed given the number of available days for the survey and the number of facilities in the sampling frame; **HF** = health facility

2.8 National guidelines

National recommendations for malaria case management are derived from a series of malaria guidelines developed by the National Malaria Control Program (MoH, 1998; 2000b), broader clinical guidelines developed by the Ministry of Health (MoH, 1994), and IMCI guidelines developed by WHO and UNICEF (Gove, 1997) and modified by the Kenyan IMCI programme (MoH, 2000a). In this study two guidelines were used as the

benchmarks for comparison because: 1) they specifically addressed case management standards for health workers at health facility level; and 2) they presented the most recent reference material, nationally recommended at the time of the survey. These two guidelines were: 1) *National Guidelines for Diagnosis, Treatment and Prevention of Malaria for Health Workers* (NMCP) (MOH, 1998); and 2) *Integrated Management of Childhood Illnesses Guideline* (IMCI) (MoH, 2000a).

The emphasis of the NMCP guideline is diagnosis and treatment standards for malaria case management across all age groups. The IMCI guideline covers assessment, diagnosis, treatment and counselling components of the clinical process within the broader aspects of the management of the sick child. It is important to acknowledge that by the time of the survey these broader quality of care standards for the management of a sick child were developed, approved at national level and reflected in IMCI guidelines, however, the dissemination of IMCI guidelines had not occurred in the surveyed districts.

2.8.1 Guidelines recommendations and study case definitions for paediatric survey

The performance standards for a health workers malaria assessment, diagnosis, treatment and counselling practices reflected NMCP and IMCI recommendations for children aged 2-59 months brought to a health facility for an initial visit. Each component of the clinical process was evaluated either on all sick children or on a subset of children and the correctness of performance was compared with these guidelines. The components of the clinical process evaluated, subsets of children analysed and definitions of the correctness of the performance are summarised in Table 2.19. The definitions were modified because some components of the NMCP guideline lacked precision and two

guidelines were not always harmonised. The following sections (2.8.1.1-2.8.1.5) describe the guideline recommendations for each component of the clinical process and present case definitions applied to measure health workers performance in the paediatric survey.

Table 2.19: Components of the clinical process evaluated, subsets of sick children analysed and definitions of the correctness of the performance

Component of the clinical process	Subsets of sick children	Performance tasks measured and definition of the correctness
1) Assessment 1	All children	Determination of age; weight; 4 general danger signs (inability to drink or breastfeed, history of convulsions, persistent vomiting, presence of lethargy or unconsciousness); fever; cough; diarrhoea; ear problem
2) Assessment 2	Children with fever	Assessment of temperature; duration of fever; anaemia; respiratory distress; dehydration; respiratory rate; previous use of drugs
3) Diagnosis	Children with fever and absent negative blood slide	Malaria diagnosis written in the patient-held record or prescription of any antimalarial drug
4) Treatment of uncomplicated malaria	Children with fever and absent negative blood slide and not referred or admitted	
A) *Drug*		
1. Recommended		Prescription of oral SP monotherapy or either SP, amodiaquine, or quinine (all as oral medications and as a monotherapy) when SP previously reported
2. Adequate		Prescription of all non-recommended antimalarials (apart from CQ or no antimalarial drug at all)
3. Inappropriate		Prescription of CQ or no antimalarial drug at all
B) *Drug and dosage*		
1. Recommended		Prescription of recommended antimalarial drug according to the recommended dose
2. Adequate		Prescription of recommended drug above or adequate drug according to or above recommended dose
3. Inappropriate		Prescription of recommended or adequate drug below recommended dose, CQ or no antimalarial drug at all
5) Treatment of severe malaria	Children with fever and absent negative blood slide and referred or admitted	
1. Recommended		Prescription of parenteral QN alone or parenteral QN with SP or QN tablets
2. Adequate		Prescription of all non-recommended antimalarial treatments (apart from chloroquine or no antimalarial treatment at all)
3. Inappropriate		Prescription of CQ or no antimalarial treatment at all
6) Counselling	Children with fever and not referred or admitted	Advice on how to give medications, extra fluids, tepid sponging, continued feeding, when to return immediately, when to come for follow up and what to do in case of vomiting
7) Communication	Children with fever and not referred or admitted	Greeting, information on diagnosis and name of medications and checking if any questions

2.8.1.1 Definitions of fever, child's initial visit, malaria and severity of illness

According to NMCP and IMCI guidelines malaria in children is defined as fever during the present illness. In the present study a child was considered to have fever if the caretaker told the interviewer that the child had fever as part of the presenting illness. After direct questioning of the caretaker, an initial visit was defined as the first visit of the sick child for this illness to this facility. An independent clinical re-examination of sick children to establish a "gold standard" diagnosis was not performed, thus the health worker's decision to manage the child as an outpatient was used as a proxy measure of uncomplicated malaria. Likewise, a health worker's decision to refer for hospitalisation was used as a proxy measure for severe malaria. Some children treated as outpatients may have had severe malaria, and thus were misclassified in the analysis; however, given that severe disease is relatively uncommon among febrile children in outpatient setting (Simoes *et al.*, 1997; Perkins *et al.*, 1997; Kolstad *et al.*, 1997), the potential bias this misclassification introduced was considered minor. Furthermore, if a child who truly had severe malaria was treated as an outpatient, or if a child who truly had uncomplicated malaria was referred for hospitalisation because the health worker thought the child had uncomplicated or severe malaria respectively, an evaluation of the child's management still provides useful information because the clinical tasks performed reflect the health worker's performance in managing uncomplicated and severe malaria.

Therefore, in the analysis malaria was defined as a history of fever during the present illness (according to the study interviewers) in the absence of a negative blood slide (according to the record in patient-held cards). In addition, treatment of the child as an

outpatient, or referral of child for hospitalisation (according to the observed health worker) was used as the criterion to distinguish uncomplicated from severe malaria.

2.8.1.2 Definitions of assessment tasks

The performance of assessment tasks was evaluated for children with fever and for all children regardless of the presence of fever, according to assessment tasks stated in NMCP and IMCI guidelines. The list of assessment tasks promoted by both guidelines is presented in Table 2.19. All children, regardless of the presence of fever, were included in the analysis to evaluate health workers performance in assessing IMCI recommended "general danger signs" (inability of child to drink or breastfeed, history of convulsions, persistent vomiting and presence of lethargy or unconsciousness) and signs of other most common diseases (cough, difficult breathing, diarrhoea and ear problem). Assessment tasks were judged as correct if the health worker "determined" that the child had a particular symptom. "Determined" refers to whether the health worker asked about the presence of the symptom or the caretaker spontaneously reported the symptom. This definition prevented health worker's performance being judged as incorrect when the presence of the symptom was already available to the health worker.

2.8.1.3 Definitions of correct malaria diagnosis

In "high malaria risk areas" (defined according to IMCI as $\geq$5% of childhood fevers caused by malaria), all children with fever or history of fever should be classified as having malaria. The IMCI guideline does not consider blood smear results. The NMCP guideline is in accordance with IMCI recommendations where microscopy is not available. However, at facilities with a functional laboratory, NMCP guidelines promote

the use of microscopy but remain ambiguous about what to do when a child with a fever has a negative blood smear. To prevent health workers practices being judged as incorrect due to guideline ambiguities on the interpretation of microscopy, when the correctness of diagnostic and treatment practices was analysed, patients with negative blood smear results were excluded. A detailed analysis on how the availability of microscopy affected malaria case management is presented in Chapter 6. Since all of our surveyed districts and facilities belong to "high malaria risk areas", "correct" malaria diagnostic practice was defined as malaria diagnosis written in the patient-held record or prescription of any antimalarial drug for the febrile child. This adjustment was done since a substantial number of patients (6%) did not have any diagnosis written in their cards but all of them had medications prescribed. This definition prevented health workers diagnostic performance being judged as incorrect when it was obvious that a malaria diagnosis was considered when antimalarial treatment was prescribed.

2.8.1.4 Definitions of correct treatment practices

For uncomplicated malaria, both IMCI and NMCP guidelines recommend oral SP as the first-line treatment and oral amodiaquine or quinine as the second-line treatment. However, the guidelines do not specify if health workers should prescribe second-line drugs if the child had received treatment at home with SP. For SP and amodiaquine, the NMCP and IMCI guideline specify ranges of appropriate dosages according to the patient's age and weight. Both guidelines give concordant recommendations with regard to amodiaquine dosages; however, the recommendations for SP dosages in children 1-3 years old are not harmonised between two guidelines. Furthermore, the IMCI guideline recommends use of oral quinine as second-line treatment but does not specify appropriate

dosages. The dosage recommendations for nationally recommended antimalarials are presented in Tables 2.20, 2.21 and 2.22.

Table 2.20: NMCP and IMCI guideline recommendations for the use of SP tablets

NMCP guideline				IMCI guideline		
Age group	Weight range (kg)	Total SP as single dose		Age group	Weight range (kg)	Total SP tablets as single dose
		Tablets	Drops			
< 3 months	< 5	¼	12 [a]	2-11 months	4 – 10	½
3 – 11 months	5 – 9	½	20			
1 – 3 years	10 – 14	¾	30	1-3 years	10 – 14	1
4 – 6 years	15 – 18	1	45	3 – 5 years	14 – 19	1
7 – 11 years	19 – 37	1 ½	NA	NA	NA	NA
12 – 15 years	38 – 49	2 ½	NA	NA	NA	NA
16 + years	50 +	3	NA	NA	NA	NA

[a] 12 drops of SP are recommended for children below 6 months or below 7 kg; **NA** = not applicable

Table 2.21: NMCP and IMCI guideline recommendations for the use of AQ preparations

Age group	Weight range (kg)	No of tablets 200 mg base or mls of syrup 50 mg base[a]							
		Day 1		Day 2		Day 3		Total	
		Tabs	mls	Tabs	mls	Tabs	mls	Tabs	mls
< 6 months	< 7	¼	7.5	¼	7.5	¼	5	¾	20
6 – 11 months	7 – 9	½	10	½	10	¼	5	1 ¼	25
1 – 3 years	10 – 14	¾	15	¾	15	½	7.5	2	37.5
4 – 5 years	15 – 18	1	20	1	20	½	10	1 ½	50
6 – 12 years	19 – 37	1 ½	1 ½	1 ½	NA	¾	NA	3 ¾	NA
13 – 15 years	38 – 49	2 ½	2 ½	2 ½	NA	1 ¼	NA	6 ¼	NA
16 + years	50 +	3	3	3	NA	1 ½	NA	7 ½	NA

[a] Syrup preparations are only recommended by NMCP guideline; **mls** = millilitres; **NA** = not applicable

Table 2.22: NMCP guideline recommendations for the use of quinine tablets

Age group	Weight range (kg)	No of tablets per dose given 8 hourly	
		Quinine Sulphate 200 mg	Quinine Bisulphate 300 mg
< 3 months	< 5	¼	¼
3 – 11 months	5 – 9	½	½
1 – 3 years	10 – 14	¾	¾
4 – 5 years	15 – 18	1	1
6 – 7 years	19 – 25	1 ¼	1 ¼
8 – 12 years	26 – 37	1 ¾	1 ¾
13 – 15 years	38 – 49	2 ½	2 ½
>16 years	50 +	3	3

Three outcome categories were used to evaluate "correctness" of treatment practice for uncomplicated malaria: 1) "recommended", defined according to national guidelines; 2) "adequate" or "minor errors", treatment not in accordance with national guidelines, but judged to have about the same efficacy as the recommended treatment; and 3) "inappropriate", treatment not belonging to any of the above two categories. This analytical approach separates non-recommended practices into two different categories, because each of them may have different clinical consequences. Therefore, as opposed to non-effective treatment ("inappropriate"), antimalarial treatment that is effective but not recommended by national guidelines ("adequate") should not increase a child's risk of developing severe malaria and death.

To define three outcome categories of the "correctness" of treatment practice two types of drug-related parameters were used to perform two separate analyses: 1) analysis based on the choice of antimalarial drug only; and 2) analysis based on the choice of drug and appropriateness of its dosage. Although not the only one, the choice of drug is the critical component of treatment quality and from a programmatic point of view the antimalarial prescription pattern is of particular importance for the policy makers. However, in the second analysis, the criterion of dosage was added because even if a drug is selected according to national guidelines its prescription below the recommended dose may present inappropriate treatment, compromise treatment quality and may have dangerous clinical consequences.

To perform the analysis of the "correctness" of treatment practice based on the choice of antimalarial drug, three treatment categories were defined: 1) "recommended", prescription of oral SP monotherapy; in addition, to prevent health workers' practices from being judged as incorrect due to imprecision of the guidelines, if the caretaker reported during the consultation that the child's illness had already been treated with SP, the prescription of either SP, amodiaquine, or quinine (all prescribed as an oral medication and as a monotherapy) was considered "recommended" treatment; 2) "adequate" or "minor error", prescription of all non-recommended but still effective antimalarial drugs; and 3) "inappropriate", prescription of either chloroquine or no antimalarial drug at all.

To perform the analysis of the "correctness" of treatment practice based on the choice of antimalarial drug and appropriateness of its dosage, the 3 treatment categories were defined: 1) "recommended", prescription of recommended antimalarial drug according to the recommended dose; 2) "adequate" or "minor error", prescription of recommended drug above, or adequate drug given according to or above the recommended dose; if two antimalarial drugs were prescribed "adequate" treatment was considered present if one or both drugs were prescribed according to or above the recommended dose; and 3) "inappropriate", prescription of recommended or adequate drug below recommended dose (condition necessary for both drugs if two antimalarials are prescribed), prescription of chloroquine regardless of the dose or no antimalarial drug at all. With regard to the SP dosages, to prevent health worker's treatment practices being judged as "inappropriate" due to the discordant recommendations between NMCP and IMCI guidelines, the

recommendations from NMCP guideline were used as the gold standard and the dosage of ¾ tablet was considered as the recommended treatment for the child aged 1-3 years.

For severe malaria, parenteral quinine is recommended by both guidelines, intramuscular as a part of pre-referral management before hospitalisation and parenteral (intravenous drip or intramuscular) in the inpatient setting. Therefore, "recommended" treatment was defined as prescription of any parenteral quinine for the patient referred for hospitalisation. An adequate treatment was defined as the prescription of all non-recommended but still effective antimalarial treatments. Inappropriate treatment was defined as either chloroquine or no antimalarial treatment.

2.8.1.5 Definitions of counselling tasks

The NMCP guideline does not provide recommendations on the counselling component of the clinical process. To evaluate health workers counselling and communication performance, the IMCI recommended tasks for febrile children treated on an outpatient basis were used as the gold standard. The list of counselling and communication tasks recommended by the IMCI guideline is presented in Table 2.19.

2.8.2 Guideline recommendations and case definitions for older children and adult survey

Unlike for children below 5 years of age, the national guidelines provide limited case management instructions for children aged above 5 years and adults. The IMCI guideline, by definition, does not address patients above 5 years of age whilst the NMCP guideline provides only a small and inconsistent section for the management of patients in the same

age group. In older children and adults, the NMCP guideline recommends clinical diagnosis of malaria in patients with fever or history of fever, chills, rigors, headaches, joint aches and pains in the absence of other causes of fever. However, the guideline does not specify what clinical assessment tasks health workers should perform and what signs and symptoms present sufficient clinical criteria for other causes of fever. The guideline does not make any age distinction when it comes to the use and interpretation of malaria microscopy, implying that the same ambiguous recommendations are valid as for children below 5 years of age (Section 2.8.1.3). There are no recommendations provided on the counselling component of the clinical process while the treatment recommendations are the same as for children below 5 years of age (Section 2.8.1.4).

Given the lack of specified clinical standards and lower malaria risks in this age group compared to young children (Section 1.3.5.4), the focus of the older children and adults survey was not primarily an evaluation of the health workers practices in accordance with guidelines but a broader description of the current practices in clinical assessment of febrile patients, the accuracy of the routine health workers diagnosis of malaria, a description of the use and interpretation of microscopy, and the ability of clinical signs and symptoms to predict *P. falciparum* infection in febrile older children and adults.

2.8.2.1 Definitions of fever and malaria

A patient above 5 years of age was considered to have fever if a history of fever was reported in the last 48 hours or axillary temperature was ≥37.5 °C. History of fever was recorded as "main complaint" if it was spontaneously mentioned in response to a general

question as to the reason for presentation to the clinic or "prompted" if it was reported on subsequent systematic questioning by the study physician during the exit examination.

To evaluate the accuracy of the routine health workers' diagnosis of malaria, a "true" case of malaria was defined as a patient presenting with fever and detectable parasitaemia of any level and species determined by two expert microscopists during the post-survey reading of malaria slides. This definition is a conservative one, as fever and parasitaemia are common among sick outpatients but are not necessarily causal. However, this is a valid case definition at health facilities with microscopy, as most case management guidelines would use fever and parasitaemia as an indication for antimalarial treatment.

To assess the ability of clinical signs and symptoms to predict *P. falciparum* infection in febrile older children and adults a "true" case of malaria was defined as a patient presenting with fever and *P. falciparum* parasitaemia of any level.

2.8.2.2 Definitions of clinical assessment tasks

To evaluate the quality of health workers clinical assessment for patients with fever, the list of various clinical assessment tasks was developed and separated into three groups: 1) the tasks related to general information such as determination of age, weight, previous use of drugs and whether the visit was initial or follow up; 2) the tasks related to the signs and symptoms traditionally associated with malaria (headache, chills, shivering, joint pains, backache, anaemia and splenomegaly); and 3) the tasks related to the signs and symptoms commonly associated with other causes of fever than malaria (cough, running

nose, difficulties in breathing, chest pain, abnormal chest sound, throat problem, ear problem, urinary problem, lymphadenopathy, diarrhoea and vomiting). The performance of clinical evaluation tasks was judged as "determined" in relation to the health workers intention to detect various signs and symptoms. To prevent health worker's performance of assessment tasks being judged as inadequate when the presence of the symptom or sign was already available to the health worker, a symptom was judged as "determined" if health worker asked about its presence or the patient spontaneously reported the symptom. Likewise, a sign was judged as determined if health worker performed the task or the surveyor could obviously tell the patient had the information of interest during the observation of consultation.

2.9 Data collection forms

2.9.1 Data collection forms for paediatric survey

Data collection forms were developed to capture information on the management of malaria and fevers as articulated in NMCP and IMCI guidelines, as well as health facility and health worker characteristics, considered important to support adequate malaria case management. Five survey forms were developed: 1) direct observation (Appendix I); 2) exit interview (Appendix II); 3) caretaker interview (Appendix III); 4) health worker interview (Appendix IV); and 5) health facility assessment (Appendix V).

The direct observation form (Appendix I) was developed to capture data on health workers performance of assessment and counselling tasks during consultations for paediatric patients. The data were collected by a silent observer who recorded the

performance of clinical tasks using a checklist. Exit and caretaker interview forms (Appendices II and III) were developed to collect data about the child's age, history of fever, previous use of antimalarial drugs, counselling and drug dispensing practices outside the consultation room, and if the visit was an initial or follow up consultation. In addition, information was collected from patient-held records about diagnostic procedures requested and results reported (i.e. malaria blood smears), medications prescribed, and if the child was treated as an outpatient or referred for hospitalisation. Interviews with caretakers were performed when they were ready to leave the facility.

The health worker interview form (Appendix IV) was developed to collect data on health workers demographics, pre-service training, working experience, possession of the guidelines, and exposure to in-service training and supervision. The health worker interview was performed with the observed clinician at the end of the health facility visit. The health facility assessment form (Appendix V) was developed to collect data on the availability of medical supplies and equipment related to malaria case management. All paediatric forms were pre-tested by the survey trainers and myself on 100 sick child consultations and 5 health workers at Upendo Dispensary in Nairobi.

2.9.2 Data collection forms for older children and adult survey

Four survey forms were developed to capture the performance of clinical assessment tasks for febrile older children and adults but also to assess practices related to the use and interpretation of microscopy, the accuracy of the routine health workers diagnosis of malaria and to assess in greater depth the ability of signs and symptoms to detect *P.*

falciparum infection among a febrile outpatient population. The survey forms were: 1) direct observation (Appendix VI); 2) temporary patient card (Appendix VII); 3) exit examination (Appendix VIII), and 4) health worker interview (Appendix IX).

The direct observation form (Appendix VI) was developed to capture data on health workers performance of assessment tasks during consultations for patients older than 5 years of age. The form was developed to reflect clinical standards considered either common or clinically important for malaria case management in this age group. The data were collected by the silent observer who recorded the performance of clinical tasks using a checklist.

The temporary patient card (Appendix VII) is the form where the observed clinicians recorded the clinical notes during the consultations of enrolled patients. Information about health workers routine practices such as medications prescribed, diagnostic procedures requested and results reported were collected from this form. The structured exit examination form (Appendix VIII) was developed to establish in greater depth the presence of signs and symptoms during the re-examination of patients by the study physician. The health worker interview form (Appendix IX) was developed to collect data on health workers demographics, pre-service training, working experience, possession of guidelines, and exposure to in-service training and supervision.

2.10 Survey teams and training of surveyors

2.10.1 Survey teams and training of surveyors for paediatric survey

The paediatric survey work in each of the four districts was conducted with four teams composed of three surveyors supervised by a clinician from the DOMC and myself who also acted as trainers. Each team consisted of a clinical officer who performed observations of consultations, health worker interviews and health facility assessments, and two nurses who performed interviews with caretakers. Clinical officers and nurses were recruited in the surveyed districts to ensure that all are familiar with the local vernacular languages. The clinicians who trained the surveyors supervised the survey teams during the facility visits to ensure that the survey protocol was correctly followed.

The training of surveyors was conducted over three days the week prior to the survey with patients and caretakers presenting at the outpatient departments of district hospitals. The training consisted of: 1) general introduction to the purpose and design of the survey; 2) instruction and practice interviewing caretakers; 3) instruction and practice observing and recording a health worker examining different children; and 4) problem solving and role-playing to assure accuracy of data collection.

To assess the surveyors' ability to accurately observe consultations (for observers) or record caretaker responses (for interviewers), the role-plays of consultations and interviews were conducted in which a "gold standard" set of correct observations (or interview responses) was determined by the trainers. For each role-play, a percent agreement score was calculated for each surveyor, where percent agreement = (number of

survey items the surveyor recorded that matched the gold standard / total number of survey items for a particular role-play) x 100%. Training continued until the agreement scores were greater than 90%. On the fourth day of the training, a full field trial of the survey tools and procedures was conducted in four facilities not selected as part of the survey.

2.10.2 Training of surveyors for older children and adult survey

The older children and adult survey work in each of the two districts was conducted with one survey team composed of three surveyors supervised by myself. Each team consisted of a clinical officer who performed observations of consultations and health worker interviews, a study physician who performed exit examination, and a laboratory technician who prepared malaria slide for febrile patients. I stayed permanently at the health facility during the survey visits and supervised the team ensuring that the survey protocol was correctly followed.

The selected personnel for older children and adult surveys were the same surveyors who previously participated in the paediatric survey and showed the best performance. Before the actual survey the training and accuracy testing was performed following the same content and procedures as in the paediatric survey. Training and accuracy testing was undertaken over three days in each district hospital until agreement of practice was greater than 90%, for both observer and exit examiner.

2.11 Survey procedures

2.11.1 Survey procedures for paediatric survey

Prior to the surveys, I visited each of the DHMTs, presented the survey and requested their cooperation. The week prior to the survey, the initial GIS sampling frame was adjusted with DHMT members, the average number of sick children seen per day was counterchecked with estimates extrapolated from monthly reports and sampling of facilities was performed (Sections 2.6 and 2.7). In the same week, a representative of the DHMT and myself visited the in-charges of each selected health facility and requested their assistance during the survey. The in-charge of the facility was told that the DOMC and DHMT were observing how malaria related care is currently provided as part of monitoring and evaluation activities of DOMC. He/she was advised that the results were confidential and would not be used in any punitive way. The exact day of the survey visit was not announced in advance to the facility staff.

On the day of the survey, survey teams arrived at each facility without prior notice, before the official opening time (8:00 a.m.) and stayed until the official closing time (5:00 p.m.) or until the time when the night shift would take over duties in facilities opened 24 hours. Each survey team carried with them a letter from the Ministry of Health specifying the purpose and nature of the survey. After obtaining consent from the facility in-charge and introducing themselves to facility staff, the team asked for a brief tour of the facility and worked with the staff to establish posts for observation and interviews with caretakers and health workers. After the observed health worker and caretaker (usually the child's mother) consented verbally, an observer recruited all sick children

presenting to the outpatient departments during working hours. If more than one health worker was seeing sick children at a facility, all were observed and interviewed.

The data were collected using four methods in the following order. First, the surveyor silently observed consultations using the direct observation form. Second, caretakers were interviewed using exit and caretaker interview form when they were ready to leave the facility. Third, interviews were conducted with observed health workers at the end of the two-day survey visit. Fourth, a health facility assessment was performed with the facility in-charge either at the end of the working day or during the time when there were no patients at the facility.

Before leaving the facility, the team members reviewed all data forms for blanks, inconsistencies and illegible writing. After the second day of the survey, the supervisor provided confidential and constructive feedback to the facility's in-charge and health workers. The team then thanked the facility staff and departed.

2.11.2 Survey procedures for older children and adults survey

The survey procedures prior to the facility visits were the same as in the paediatric survey (Section 2.11.1). Verbal consent from the observed clinician was sought prior to the commencement of the survey procedures. In particular it was explained that an evaluation of the overall picture of care was the aim, that an individuals performance was not being judged and that the aim was not to highlight or punish an individuals "poor performance". The observer and myself carried out initial screening of all sick patients

above 5 years of age presenting at the waiting area of an outpatient clinic between 8 a.m. and 5 p.m. Patients presenting with trauma, burns, chronic follow up conditions or routine antenatal visits were excluded. Prior to the observations the patients or caretakers were provided with a consent information sheet and the study was explained in the language they felt most comfortable with (Appendix X). The informed written consent was obtained for all recruited patients (Appendix XI).

The data were collected using four methods in the following order. First, the surveyor silently observed consultations using the direct observation form. The observed health worker performed consultations as per usual procedure and recorded the patient's clinical notes in the temporary patient card that remained in the consultation room.

Second, the study physician located in a separate examination room re-examined all the patients using the exit examination form without seeing the temporary patient card completed during the first consultation. In addition, the study physician recorded clinical notes, diagnosis and medications into patient-held records as per routine facility procedures.

Third, a finger-prick blood sample for malaria microscopy was taken at the exit examination by the study laboratory technician if the patient had an axillary temperature $\geq$37.5°C or reported a history of fever in the last 48 hours. Thick and thin blood films were prepared at the facility and stained with Giemsa 10%. If a blood film was requested during the initial health worker consultation the study malaria slide was prepared

simultaneously in the facility's clinical laboratory. During the post-survey work two independent expert microscopists examined all collected slides at the KEMRI/Wellcome Trust laboratories in Nairobi and the number of parasites per 200 white blood cells (WBC) was counted. Parasite density/μl of blood was calculated assuming an average leukocyte count of 8,000 WBC/μl of blood.

Fourth, interviews were conducted with observed health workers at the end of the two-day facility visit. Before leaving the facility, team members reviewed all data forms to ensure they were complete and correct and provided confidential and constructive feedback to the facility's in-charge and health workers regarding specific assessment, diagnosis and treatment steps. The team then thanked the facility staff and departed.

2.12 Data entry, management and storage

Data entry and validation were undertaken using Microsoft Access 2000 (Microsoft Inc, Redmond, Washington) through customised data entry screens with in-built range and consistency checks. All forms were entered twice by independent data entry clerks and completed data sets were compared for data-entry errors. All data entry and management was undertaken at the KEMRI/Wellcome Trust Programme in Nairobi and data stored on PCs and on CDROMs at this centre.

2.13 Statistical analysis

2.13.1 Statistical analysis of the children's survey

All analyses were performed using STATA, version 6.0 (StataCorp, College Station, Texas). The major analyses of the children survey were descriptive and included an analysis of predictors of treatment practice in accordance with guidelines.

2.13.1.1 Descriptive analysis

Descriptive analysis of the health worker performance indicators was performed for each district and combined for four districts across the two facility type strata. The results are presented aggregated for four districts and all types of facility if significant differences between districts or between types of facility within four districts were not observed (Chapter 3). Descriptive analysis of the health workers practices from facilities with functional microscopy was performed for four districts together and across two age groups (< 1 year and 1-4 years) (Chapter 6). In each analysis the precision of proportions (95% confidence interval) was estimated accounting for the cluster sampling design by defining all sick child consultations occurring at a surveyed health facility as the primary sampling unit. To account for unequal probabilities of selection of health facilities, sampling weights were applied when results from different strata were combined. The weights were calculated as the inverse probability of selection of the health facility (Table 2.23).

Table 2.23: Distribution of sampling weights across districts and strata

District	No of HFs in sampling frame	No of surveyed facilities	Probability of HFs selection[a]	Weight[b]
KWALE				
Dispensaries	36	15	0.42	2.40
HC	8	8	1	1
District Hospital	1	1	1	1
KISII				
Dispensaries	22	10	0.46	2.20
HC	13	8	0.62	1.63
District Hospital	1	1	1	1
BONDO				
Dispensaries	12	12	1	1
HC	4	4	1	1
District Hospital	1	1	1	1
MAKUENI				
Dispensaries	37	11	0.30	3.36
HC	14	9	0.64	1.56
District Hospital	1	1	1	1

[a] Probability of selection = number of surveyed facilities/number of facilities in sampling frame
[b] Weight = 1/probability of selection
HF = health facility; **HC** = health centre

2.13.1.2 Predictors analysis

The predictors analysis of the health workers treatment practices was performed on aggregated data from the four districts (Chapter 4). To identify predictors of three categories of treatment quality (recommended, minor errors, and inappropriate), multiple binomial logistic regression modeling was used (Rowe *et al.*, 2003). With this technique, a series of binomial logistic regression models were created (one model for each category of treatment quality), and the results were interpreted together. The logistic regression models were fitted with the STATA xtgee procedure using an exchangeable working correlation matrix. This procedure uses generalised estimating equations to account for the potential correlation of treatment quality among children seen by the same health worker (Horton & Lipsitz, 1999). The exchangeable correlation structure assumes the

correlation of the treatment quality between any pair of children is approximately constant.

In the univariate analysis, the odds ratio (OR), p-value, and 95% confidence interval for the association of each category of treatment quality was computed with the series of potential predictors. All logical statistical interactions were examined. To adjust for confounding, factors with a p-value <0.15 from the univariate analysis and interaction terms with p-value <0.05 were entered into three multivariate logistic regression models (as in the univariate analysis, one model for each category of treatment quality). Factors that did not initially meet the entrance criteria for the multivariate analysis (i.e. "non-significant" [p ≥0.15]) were then entered into the three multivariate models, one factor at a time. If the addition of a "non-significant" variable changed the OR of any already-included variable by >10%, the additional variable was retained in the final multivariate model. The three multivariate models were forced to contain the same variables: any variable meeting the entrance criteria for one model was automatically entered into the other two models. This approach ensured that the three ORs (one from each model) for a given factor would be adjusted for the same covariates. The list of all factors examined and statistical procedures for each variable are presented in Chapter 4.

2.13.2 Statistical analysis of older children and adult survey

The major analyses of the older children and adult survey were descriptive and predictors analysis and were performed using STATA software, version 8.0 (StataCorp, College Station, Texas).

2.13.2.1 Descriptive analysis

The major descriptive analyses in older children and adults survey were the following:

1) Analysis of the health workers clinical assessment practices (Chapter 5),
2) Analysis of the accuracy of the routine health workers diagnosis of malaria (Chapter 5),
3) Analysis of the health workers practices related to the use and interpretation of microscopy (Chapter 6), and
4) Analysis of the accuracy of the routine reading of malaria slides (Chapter 6).

The analysis of the health workers clinical assessment practices (analysis 1) was performed on the non-stratified sample for each of the two study districts (Kwale and Kisii) and overall for two districts together. Furthermore, comparative age-specific analysis on the combined data sets from the two districts was performed between two age groups (5-14 years and above 14 years). The analysis of the accuracy of the routine health workers diagnosis of malaria (analysis 2) was performed across two age-groups (5-14 years and above 14 years) at the health facilities without functional microscopy, in each district and overall for two districts together. The analysis of the health workers practices related to the use and interpretation of microscopy (analysis 3), and the accuracy of routine reading of malaria slides (analysis 4) was performed on the patients from facilities with functional microscopy, on district combined data sets and across two age groups (5-14 years and above 14 years of age).

In all descriptive analyses, the precision of proportions (95% confidence interval) was estimated accounting for the cluster sampling design by defining all consultations

occurring at a surveyed health facility as the primary sampling unit. The district-combined results stratified on the basis of the availability of microscopy did not require weighting since the probability of the selection of health facilities was equal in each district (sampling weight was 1.9 at facilities without microscopy and 1.4 at facilities with microscopy). The relative sampling weights between strata within a district were of small magnitude (1.9/1.4 = 1.36). The differences between non-stratified weighted and unweighted results were examined and were trivial (not exceeding 0.3%), not affecting interpretation of the results for any of the estimates measured. Therefore, only the unweighted results are presented.

To analyse the accuracy of the routine health workers diagnosis of malaria and the quality of the routine reading of malaria slides, parasitaemia of any level and species in the febrile patient determined by two expert microscopists was used as a gold standard. The sensitivity, specificity, and positive and negative predictive values were calculated according to the following formula:

Accuracy of the routine malaria diagnosis:

Sensitivity = Routine diagnosis of malaria / Malaria parasitaemia present

Specificity = Routine diagnosis of non-malaria / Malaria parasitaemia absent

Positive predictive value = Malaria parasitaemia present / Routine diagnosis of malaria

Negative predictive value = Malaria parasitaemia absent / Routine diagnosis of non-malaria

Quality of the routine reading of malaria slides:

Sensitivity = Routine malaria slide positive / Malaria parasitaemia present

Specificity = Routine malaria slide negative / Malaria parasitaemia absent

Positive predictive value = Malaria parasitaemia present / Routine malaria slide positive

Negative predictive value = Malaria parasitaemia absent / Routine malaria slide negative

2.13.2.2 Predictors analysis

The analysis of the ability of various signs and symptoms to detect *P. falciparum* malaria in febrile patients was performed after stratification based on the patients' age (older children vs adults); however, due to the small number of true malaria cases district specific analysis could not be performed and the data were combined from the two study districts.

The univariate analysis of the strength of association between clinical predictors and malaria was estimated using logistic regression modeling, and the odds ratios (OR) with associated p-values were calculated for each investigated sign and symptom. To adjust for confounding, clinical predictors with a p-value <0.20 from the univariate analysis were entered into two age-specific multivariate logistic regression models. Using backward elimination strategy clinical predictors independently associated with malaria (OR with p-value <0.05) were identified. To analyse the ability of an individual and a group of clinical predictors to detect *P. falciparum* malaria in a febrile patient the sensitivity, specificity, and positive and negative predictive values were calculated according to the following formula:

Sensitivity = Clinical predictor absent / *P. falciparum* infection present

Specificity = Clinical predictor absent / *P. falciparum* infection absent

Positive predictive value = *P. falciparum* infection present / Clinical predictor present

Negative predictive value = *P. falciparum* infection absent / Clinical predictor absent

2.14 Study limitations

The health facility surveys experienced several important methodological limitations. First, the presence of the study observer may have caused health workers to perform better than usual (the Hawthorn effect, as suggested by results from Benin [Rowe *et al.*, 2002]) or worse than usual, if observers made health workers nervous. Second, as explained in detail in Section 2.8.2.1, there was no clinical re-examination during the paediatric survey to provide a "gold standard" diagnosis in accordance with guidelines; therefore, we relied upon the proxy measures to classify severity of malaria diagnosis. Third, during the paediatric survey, the child's temperature was not measured during the exit interview; therefore, the case definition of a febrile child, based solely on the caretaker's history, may have underestimated the presence of malaria according to guidelines. Fourth, during the older children and adult survey, the microscopic "gold standard" diagnosis of malaria did not necessarily overcome the problem of coincidental malaria parasitaemia in a febrile patient unwell for another reason. Fifth, since multiple comparisons in all analyses were performed some differences may have been significant by chance. Conversely, the true differences for certain indicators between different strata may not have been demonstrated due to the size of design effect and inadequate sample size. Sixth, due to the small number of malaria cases, district specific analysis of clinical

predictors of malaria in older children and adults could not be performed and data from two districts had to be combined. Seventh, during the predictors analysis on the quality of the treatment in children, not all potential factors were studied such as health workers perceptions or complexity of guidelines and only limited details were available on key programmatic interventions such as supervision and training.

CHAPTER 3:

Evaluation of outpatient malaria case management in children

3.1 Introduction

Malaria case management, emphasising prompt diagnosis and effective treatment, especially in children below 5 years, forms the bedrock of malaria control in Africa (WHO, 1996a; 2000a). In East and Southern Africa, since the early 1990's, under-five malaria mortality rates have risen significantly, coincidental with the emergence of resistance to widely used first-line therapeutic chloroquine (Snow *et al.,* 2001b; Korenromp *et al.*, 2003). Countries of these regions have struggled in recent years to define affordable alternatives to the rapidly declining effectiveness of chloroquine. Drug policy revisions have been slow but now implemented in a number of East African countries (EANMAT, 2003) and South Africa (Craig *et al.*, 2004).

However, deciding to change first-line drugs is only part of a complex process aimed at improving the overall process of malaria case management. The adequate provision of good clinical practice up to the standards of care defined in evidence-based guidelines remains indispensable. Furthermore, good clinical practice requires programmatic health systems supports, which include effective training and supervision of health workers, development and dissemination of guidelines and adequate provision of antimalarial drugs.

To tackle the risks posed by malaria to broad development targets the Ministry of Health launched the Kenya National Malaria Strategy (KNMS) in April 2000. This strategic framework gives considerable importance to clinical management, with emphasis on prompt and effective treatment (DOMC, 2001). The KNMS reflects approaches

established in a series of guidelines developed during the change of treatment policy from chloroquine to SP between 1998 and 2000 (MoH, 1998; 2000b) and the more recent adoption of approaches to IMCI (Gove, 1997; MoH, 2000a).

This chapter presents the results of a series of performance indicators among government health service providers according to their ability to assess, diagnose, treat and counsel febrile paediatric patients. In addition, health systems support indicators related to malaria case management are also presented. Furthermore, these indicators, measured three years following the introduction of new malaria case management guidelines, will also serve to evaluate the progress towards the malaria case management targets at health facility level, set up optimistically by the KNMS to be above 80% and achieved by 2006.

3.2 Methods

Detailed presentation of the materials and methods used to evaluate outpatient, childhood malaria case management is provided in the following sections of Chapter 2:

1) Characteristics of the study districts (Section 2.3)
2) Development of the sampling frame (Section 2.6.1)
3) Sampling procedures (Section 2.7.1)
4) National guidelines and study case definitions (Section 2.8.1)
5) Data collection forms (Section 2.9.1)
6) Survey teams and training of surveyors (Section 2.10.1)
7) Survey procedures (Section 2.11.1)
8) Statistical analysis (Section 2.13.1)

The components of the clinical process evaluated, subsets of children analysed and definitions of the correctness of the performance are summarised in the previous chapter (Table 2.19).

3.3 Results

3.3.1 Description of the sample

The survey was undertaken at the outpatient departments of 81 government health facilities where 142 health workers were observed as they performed 1864 sick child consultations. No health worker or caretaker refused to participate in the study. However, of 1864 children, 170 caretakers (9.1%) left the health facility before the study team could interview them. These 170 consultations were excluded from the analysis. Of 142 observed health workers, interviews were conducted with 135 health workers. Seven (4.9%) health workers, who performed a total of 40 consultations, urgently left the health facility before an interview could be performed and could not be found within three days. The health facility assessment was performed for all 81 facilities. Dispensaries and combined health centres and district hospitals (HC/DH) accounted for 49% and 51% of observations, respectively. The distribution of the assessed health facilities and analysed health worker-sick child consultations across four districts and two types of facility is presented in Table 3.1.

Table 3.1: Distribution of the assessed health facilities and analysed health worker-sick child consultations across four districts and two types of facility

District	Dispensary	HC/DH	Total
KWALE			
Health facilities	15	9	24
Health workers	23	19	42
Consultations	228	204	432
KISII			
Health facilities	10	9	19
Health workers	19	19	38
Consultations	208	267	475
BONDO			
Health facilities	12	5	17
Health workers	17	11	28
Consultations	218	175	393
MAKUENI			
Health facilities	11	10	21
Health workers	13	21	34
Consultations	173	221	394
TOTAL			
Health facilities	48	33	81
Health workers	72	70	142
Consultations	827	867	1694

HC = health centre; **DH** = district hospital

3.3.2 Characteristics of sick children, health workers and health facilities

3.3.2.1 Characteristics of sick children

Among the 1694 consultations analysed, 81 (4.4%) children were younger than 2 months, 515 (29.4%) were 2-11 months and 1098 (66.2%) were 12-59 months. Infants accounted for 33.8% of consultations. The average number of participating children per health facility and health worker was 20.9 and 11.9 respectively. The age distribution of participating children is presented in Table 3.2.

Table 3.2: Age distribution of participating children

Age group (months)	N=1694 (%)
0-1	81 (4.4)
2-11	515 (29.4)
12-23	406 (24.5)
24-35	280 (16.8)
36-47	215 (13.0)
48-59	197 (11.9)

Of 1613 sick children aged 2-59 months, 1516 (94.0%) were brought to the facility for an initial consultation. The performance of the assessment tasks was evaluated on all 1516 initial visits and on the subset of 1237 initial visits of children with fever. Of 1516 initial consultations, 1103 met our definition of malaria: uncomplicated malaria accounted for 1040 (95.3%) and severe malaria for 63 (4.7%) initial consultations. Of 63 children with severe malaria, 21 (37.7%) patients were referred for hospitalisation from facilities without an inpatient department and 42 (62.3%) were admitted at facilities with inpatient services. The subsets of sick children used for the evaluation of different components of clinical process across four districts are presented in Table 3.3.

Table 3.3: Subsets of sick children across four districts[a]

Subset of children	KWALE	KISII	BONDO	MAKUENI	Total
Assessment 1	363	450	358	345	1516
Assessment 2	303	393	277	264	1237
Diagnosis	264	355	262	222	1103
Treatment of uncomplicated malaria	257	318	246	219	1040
Treatment of severe malaria	7	37	16	3	63
Counselling and communication	294	349	260	260	1163

[a] See Table 2.19 for definitions of the subsets

Fever and cough accounted for the majority (71.4% and 54.9% respectively) of the sick children's main complaints (complaints stated by caretaker without prompting), and

commonly children had both of these symptoms (41.0%). Diarrhoea, vomiting and non-specific symptoms, such as not eating well and stomach ache, were the main complaints among 13-19% of sick children. The average number of main complaints per child was 2.9. The sick child main complaints are presented in Table 3.4.

Table 3.4: Summary of the sick child's main complaints

Main complaint	N=1694 (%)	95% CI
Fever	1199 (71.4)	68.1, 74.8
Cough	898 (54.9)	49.9, 59.8
Vomiting	358 (19.1)	16.2, 22.0
Diarrhoea	261 (14.6)	12.1, 17.0
Not eating well	249 (13.9)	11.2, 16.6
Stomach ache	226 (13.4)	11.0, 15.8
Difficult breathing	198 (12.0)	9.4, 14.7
Skin problem	195 (10.2)	8.2, 12.2
Runny nose	142 (8.7)	5.9, 11.5
Malaria	69 (5.6)	2.5, 8.8
Headache	63 (3.9)	2.9, 5.0
Mouth or throat problem	58 (3.6)	2.4, 4.8
Eye problem	51 (3.0)	2.1, 3.9
Ear problem	48 (2.9)	2.0, 3.9
Convulsions	35 (2.2)	1.4, 3.0
Swellings	32 (1.8)	1.0, 2.7
Crying a lot	31 (1.6)	0.9, 2.3
Traumas	19 (1.2)	0.6, 1.7
Worms	13 (0.9)	0.4, 1.4
Constipation	17 (0.8)	0.2, 1.3
Burns	5 (0.3)	0, 0.5
No complaint	15 (0.9)	0.2, 1.6
Others	55 (2.7)	1.7, 3.8
Fever and cough	663 (41.0)	36.9, 45.2

3.3.2.2 Characteristics of health workers

Of 142 observed health workers, 135 participated in health worker interview and provided information on their demographics, exposure to in-service training, guidelines and supervision. The mean age was 38 years (range: 20-65) and the majority of the health workers were nurses (76.8%), while clinical officers (15.0%) constituted the largest

second group. Clinical officers, registered nurses (apart from one) and one doctor worked only in health centres and hospitals, while enrolled nurses and nursing aides worked mostly in dispensaries. The median health workers professional experience and the time spent in the surveyed facility were 12 years (IQR: 6-22 years), and 5 years (IQR: 3-7 years) respectively. Sixty (45.8%) health workers were in charge of the health facilities, more commonly in dispensaries than in HC/DHs. The demographics of health workers according to the type of facility are presented in Table 3.5.

Table 3.5: Demographics of health workers according to the type of facility

Health workers characteristics	**Dispensary**	**HC/DH**	**Total**
	N=71 (%)	**N=64 (%)**	**N=135 (%)**
Male sex	32 (45.8)	34 (52.0)	66 (48.0)
In-charge of health facility	44 (61.1)	16 (26.3)	60 (45.8)
Pre-service training			
Doctor	0	1 (1.9)	1 (0.7)
Clinical officer	0	29 (43.2)	29 (15.0)
Registered nurse	1 (1.5)	8 (13.1)	9 (5.6)
Enrolled nurse	62 (89.2)	23 (37.5)	85 (71.2)
Nursing aide	8 (9.3)	3 (4.3)	11 (7.6)

HC = health centre; **DH** = district hospital

No health worker received IMCI training or vertical training programmes preceding IMCI, such as trainings on the management of acute respiratory infections (ARI) or control of diarrhoeal diseases (CDD). Fifty-nine (44.9%) health workers attended in-service training on malaria. Six health workers were trained twice. About one-third of health workers who received malaria training were trained between 1998 and 1999, and about two-thirds were trained between 2000 and 2001. The duration of malaria training was 1 day for 32 (50.1%) health workers, 2–3 days for 18 (33.3%), and 5–7 days for 9 (16.6%). The malaria training course of 25 (43.8%) health workers included clinical

practice. In three out of four districts, the Ministry of Health trained the majority of health workers (93.4%) and only in Kisii district, a non-governmental organisation *Médecins Sans Frontières* trained most of health workers (83.9%). The majority (76.3%) of health workers had at least one supervision visit in the past 6 months. Of these health workers, 67.6% had 1-3 supervisory visits, 28.1% had 4-6 visits, and 4.4% had 7-10 visits. The majority (78.8%) of supervisory visit did not include observation of consultations or provision of feedback. Characteristics of health workers exposure to in-service training, guidelines and supervision according to the type of facility are presented in Table 3.6.

Table 3.6: Characteristics of health workers exposure to training, guidelines and supervision

Health workers characteristics	**Dispensary**	**HC/DH**	**Total**
HWs exposure to training, guidelines and supervision	*N=71 (%)*	*N=64 (%)*	*N=135 (%)*
HW received in-service malaria training	37 (50.3)	22 (34.8)	59 (44.9)
HW has malaria guidelines	43 (60.2)	34 (53.5)	77 (57.8)
HW had at least one supervision visit in past 6 months	62 (89.3)	32 (51.8)	94 (76.3)
Characteristics of training	*N=37 (%)*	*N=22 (%)*	*N=59 (%)*
Duration of in-service malaria training			
1 day	17 (42.8)	15 (69.9)	32 (50.1)
2-3 days	13 (37.7)	5 (27.2)	18 (33.3)
5-7 days	7 (19.5)	2 (8.9)	9 (16.6)
Type of training			
Training without clinical practice	22 (58.0)	12 (51.4)	34 (56.2)
Training including clinical practice	15 (42.0)	10 (48.6)	25 (43.8)
Characteristics of supervision	*N=62 (%)*	*N=32 (%)*	*N=94 (%)*
Number of visits in past 6 months			
1-3 visits	42 (71.8)	18 (53.9)	60 (67.6%)
4-6 visits	18 (24.8)	12 (38.7)	30 (28.1%)
7-10 visits	2 (3.4)	2 (7.4)	4 (4.4%)
Supervision performed by			
Resident HW	10 (16.7)	17 (54.4)	27 (25.6)
External HW	52 (83.3)	15 (45.6)	67 (74.4)
Type of supervision			
Supervision without observation and feedback	50 (82.1)	23 (68.2)	73 (78.8)
Supervision with observation and feedback	12 (17.9)	9 (31.8)	21 (21.2)

HC = health centre; **DH** = district hospital; **HW** = health worker

3.3.2.3 Characteristics of health facilities

SP was in stock on the day of survey in 80 of 81 facilities while either amodiaquine or quinine was available in 53.1% of facilities, more commonly in HC/DHs than in dispensaries. Injectable quinine was available in only 32.7% of facilities. Chloroquine was still available in the majority (64.3%) of health facilities. Malaria treatment wall charts were exposed in consultation rooms of 27.0% of facilities. The characteristics of health facilities according to the type of facility are presented in Table 3.7.

Table 3.7: Characteristics of health facilities

Health facility characteristics	**Dispensary** *N=48 (%)*	**HC/DH** *N=33 (%)*	**Total** *N=81 (%)*
Malaria treatment wall chart in the consultation room	10 (22.2)	12 (38.9)	22 (27.0)
SP (any formulation) in stock	47 (96.8)	33 (100)	80 (97.7)
Amodiaquine (any formulation) in stock	11 (26.6)	15 (45.8)	26 (32.1)
Quinine tablets in stock	4 (8.4)	14 (42.1)	18 (18.1)
Injectable quinine in stock	15 (33.3)	11 (31.0)	26 (32.7)
Chloroquine (any formulation) in stock	29 (68.3)	18 (54.2)	47 (64.3)
Any formulation of amodiaquine or quinine in stock	20 (46.0)	23 (68.5)	43 (53.1)

HC = health centre; **DH** = district hospital; **SP** = sulfadoxine-pyrimethamine

3.3.3 Duration and timing of consultations and distribution of patients time at the facility

The duration of consultation ranged from less than one minute to 35 minutes. Twenty-two percent of consultations were shorter than 3 minutes, while only 3.2% were longer than 10 minutes. Nearly half (48.3%) of consultations lasted 3-5 minutes. Consultations were not evenly distributed throughout the day: 82.9% occurred between 9:00 a.m. and 1:00 p.m., 16.7% after 1:00 p.m. and only 0.1% before 9:00 a.m. The median consultation time was 4.0 minutes (IQR: 3-6 minutes). No significant difference in the duration of consultation and their timing was observed between districts or between types

of facility. The distribution of duration and timing of consultations is presented in Table 3.8.

Table 3.8: Duration and timing of consultations

Duration and Timing	N=1694 (%)
Duration of consultation	
< 3 min	376 (22.2)
3-5 min	819 (48.3)
6-10 min	445 (26.3)
> 10 min	54 (3.2)
Timing of consultation	
< 9:00 a.m.	1 (0.1)
9:00 a.m. - 10:00 a.m.	177 (10.1)
10.00 a.m. – 1:00 p.m.	1233 (72.8)
> 1:00 p.m.	283 (16.7)

The majority of patients (79.6%) arrived at the facility between 9:00 a.m. and 1:00 p.m., 10.5% arrived before 9:00 a.m. and only 9.8% came to the facilities after 1:00 p.m. Within 30 minutes of their arrival, 27.2% of patients were attended, while 20.1% waited for more than 2 hours before being seen. Sixty-seven percent of patients spent less than 2 hours at the facility, however, a significant proportion of patients (15.6%) spent more than 3 hours. The median time patients waited to be attended and total time spent at the facility was 60 minutes (IQR: 87-115 minutes) and 81 minutes (IQR: 39-142 minutes) respectively. No significant difference in the distribution of patient's time at the facility was observed between districts or between types of facility. The distribution of patient's time at the health facility is presented in Table 3.9.

Table 3.9: Distribution of patient's time at health facility

Patient's time at facility	N=1694 (%)
Arrival time	
< 8:00 a.m.	21 (1.2)
8:00 – 9:00 a.m.	158 (9.3)
9:00 – 10:00 a.m.	322 (19.0)
10:00 a.m. – 1:00 p.m.	1027 (60.6)
> 1:00 p.m.	166 (9.8)
Waiting time before consultation	
< 30 min	461 (27.2)
30 min - 1h	373 (22.0)
1h - 1h30min	306 (18.1)
1h30min - 2h	214 (12.6)
> 2h	340 (20.1)
Total time spent at health facility	
< 1 h	630 (37.2)
1 - 2 h	505 (29.8)
2 - 3 h	294 (17.4)
3 - 4 h	138 (8.1)
> 4h	127 (7.5)

3.3.4 Characteristics of clinical process

3.3.4.1 Assessment

Among 1516 initial consultations for sick children aged 2-59 months, health workers determined the age and weight for 90.7% and 52.7% of children, respectively. Apart from determining whether a child was awake or alert, IMCI proposed "general danger signs" were rarely assessed (5.1-9.5%). Presence of fever was determined for the majority of patients (88.1%), more frequently than cough or difficult breathing (67.5%), diarrhoea (29.6%) or ear problems (4.9%). Apart from asking for fever (47.8%), explorative history tasks such as asking for cough or difficult breathing, diarrhoea and ear problem were rarely done for the patients not voluntarily presenting these symptoms as main complaints (1.9-23.1%).

Among 1237 children with fever the temperature was either measured or the hotness of body was felt for 62.1% of children. Duration of fever and assessment of anaemia were performed for 69.3% and 53.3% of children respectively. Assessment of patients with fever for the signs of suspected severe malaria by assessing for respiratory distress (looking at chest indrawing or deep breathing, counting breaths) and dehydration (pinching the skin) was rarely performed (0-9%). Previous use of drugs was inquired in 42.2% of children and whether a visit was an initial or follow up visit was determined in 18.2% of febrile children. No significant difference in the performance of assessment tasks was observed between districts or between types of facility. The results of assessment practices are presented in Table 3.10.

Table 3.10: Assessment tasks performed for children aged 2-59 months who were brought to an outpatient facility for an initial consultation

Assessment task	No (%)	95% CI
For all children (N=1516)		
Health worker determined[a] if the child		
Had convulsions	60 (5.1)	3.1, 7.2
Was lethargic or unconscious	1438 (94.7)	92.3, 96.4
Was unable to drink or breastfeed	143 (9.5)	6.4, 12.6
Vomited everything	104 (7.9)	4.7, 11.2
Health worker determined[a] if the child had		
Fever (by history, feeling or measuring)	1323 (88.1)	85.2, 90.9
Fever (by feeling hotness of the body)	678 (40.3)	32.0, 48.6
Fever (by measuring temperature)	403 (28.4)	18.9, 37.9
Cough or difficult breathing	998 (67.5)	63.4, 71.6
Diarrhoea	455 (29.6)	24.6, 34,7
An ear problem	70 (4.9)	3.6, 6.2
For children with fever (N=1237)		
Health worker checked		
Temperature (by measuring or feeling)	793 (62.1)	52.9, 71.3
Temperature by measuring	368 (31.7)	21.3, 42.2
Hotness of the body by feeling	581 (42.9)	34.2, 51.5
Duration of the fever by asking	875 (69.3)	60.3, 78.3
Conjunctival pallor	727 (52.9)	44.1, 61.8
Palmar pallor	54 (4.7)	1.3, 8.1
Anaemia (conjunctival or palmar pallor)	731 (53.3)	44.6, 62.0
Chest indrawing by observing the chest	87 (9.4)	4.0, 14.8
Respiratory rate by counting breaths	2 (0.2)	0, 0.5
Dehydration by pinching the skin	37 (2.3)	1.0, 3.6
Previous use of drugs by asking	556 (42.2)	33.6, 50.7

[a] Determined refers to whether the health worker was exposed to information (i.e. either asked for the information or caretaker spontaneously reported the information or the surveyor could obviously tell the child had the information of interest); **CI** = confidence interval

3.3.4.2 Diagnosis

Malaria accounted for the majority of all diagnoses made by health workers (67.8%), followed by upper respiratory tract infections (35.1%), diarrhoeal diseases (6.6%), worms (6.2%) and skin infections (4.6%). Non-specified respiratory tract infections and lower respiratory tract infections were both present in 4.7% of patients. All other diagnoses were made in less than 3% of patients. Pattern of diagnosis did not show any significant

differences between types of facility or between the districts. A summary of diagnoses is presented in Table 3.11.

Table 3.11: Summary of diagnoses made by health workers

Diagnosis	N=1694 (%)	95% CI
Malaria	1170 (67.8)	60.8, 74.8
Upper respiratory tract infection	565 (35.1)	29.0, 41.1
Diarrhoea	120 (6.6)	4.5, 8.6
Worms	107 (6.2)	4.1, 8.2
Respiratory tract infection (not specified)	85 (4.7)	2.3, 7.2
Lower respiratory tract infection	81 (4.7)	3.2, 6.2
Skin infections	88 (4.6)	3.5, 5.8
Eye infection	40 (2.4)	1.6, 3.2
Otitis	37 (2.4)	1.4, 3.3
Bronchitis	30 (2.3)	0.9, 3.6
Anaemia	40 (2.0)	1.1, 2.9
Oral thrush	34 (1.7)	0.9, 2.6
Trauma	24 (1.4)	0.8, 2.0
Abscess and cellulitis	20 (1.1)	0.5, 1.6
Malnutrition	14 (0.8)	0.3, 1.3
Tonsillitis	12 (0.7)	0.2, 1.2
Asthma	12 (0.6)	0.2, 1.0
Urinary tract infection	12 (0.6)	0.2, 1.0
Bloody diarrhoea	11 (0.5)	0, 1.0
Chickenpox	8 (0.4)	0.1, 0.6
Others	83 (4.5)	3.2, 5.7
Not written	96 (6.6)	2.0, 11.3

CI = confidence interval

Adherence of malaria diagnosing practices with NMCP and IMCI guidelines was high. Among 1103 initial consultations of febrile children aged 2-59 months, diagnosis of malaria was correct in 89.3% (95% CI: 84.2-94.4) of observations (definition of correctness is in Section 2.8.1.3). No significant difference in health workers diagnosing practices was observed between districts or between types of facility.

3.3.4.3 Treatment for uncomplicated malaria

The "correctness" of treatment was defined in three categories (recommended, adequate and inappropriate) based either on the choice of antimalarial drug only, or on the choice of antimalarial drug and appropriateness of the dosage (see definitions in Section 2.8.1.4). With regard to the choice of antimalarial drug, among 1040 children with uncomplicated malaria recommended treatment was prescribed for only 55.3% children. However, adequate treatment was prescribed for a further 30.2% of children. No significant difference was observed between districts, while differences in treatment practices were observed between types of facility. Health workers prescribed recommended treatment more commonly in dispensaries (65.1%) than in HC/DHs (34.7%). The results on the correctness of treatment based on the choice of drug for uncomplicated malaria according to the type of facility are presented in Table 3.12.

Table 3.12: Correctness of treatment based on the choice of drug for children aged 2-59 months who were brought to an outpatient facility for an initial consultation with uncomplicated malaria: results according to the type of facility

Correctness of treatment[a]	Dispensary (N=596)		HC/DH (N=444)		Total (N=1040)	
	No (%)	95% CI	No (%)	95% CI	No (%)	95% CI
Recommended[b]	420 (65.1)	53.6, 76.6	163 (34.7)	25.2, 44.2	583 (55.3)	45.9, 64.8
Adequate	118 (23.5)	14.0, 33.0	209 (44.2)	28.9, 59.5	327 (30.2)	21.9, 38.5
Inappropriate	58 (11.4)	5.7, 17.0	72 (21.1)	6.2, 35.9	130 (14.5)	8.2, 20.8

[a] See Section 2.8.1.4 for definitions
[b] This category contains only SP monotherapy prescriptions, apart from 4 children where previous use of SP was reported and amodiaquine monotherapy was prescribed
HC = health centre; **DH** = district hospital; **CI** = confidence interval

Although SP monotherapy was the most common treatment prescribed for patients with uncomplicated malaria (55.1%), six other antimalarial drugs were prescribed either as monotherapies or in combination with other antimalarials. SP monotherapy was more

commonly prescribed in dispensaries (65.1%) than in HC/DHs (33.9%). Conversely, amodiaquine, quinine and other antimalarial drugs, apart from chloroquine, were more frequently used in HC/DHs than in dispensaries, prescribed either alone or in combinations with SP. In summary, 77.1% of antimalarial treatments were prescribed as monotherapies while 22.9% were prescribed as two antimalarial drug combinations. The pattern of antimalarial drug prescriptions for uncomplicated malaria according to the type of facility is presented in Table 3.13.

Table 3.13: Antimalarial drugs prescribed for children aged 2-59 months who were brought to an outpatient facility for an initial consultation with uncomplicated malaria: results according to the type of facility

Antimalarial prescription	Dispensary (N=596)		HC/DH (N=444)		Total (N=1040)	
	No	%	No	%	No	%
SP	420	65.1	159	33.9	579	55.1
SP + chloroquine	60	11.6	30	5.5	90	9.7
Amodiaquine	8	1.3	57	13.0	65	5.1
SP + quinine	25	4.9	38	8.6	63	6.1
Quinine	13	2.8	25	6.1	38	3.7
SP + amodiaquine	2	0.3	29	5.1	31	1.9
Chloroquine	18	4.4	4	0.6	22	3.2
Artemisinins	0	0	16	2.9	16	0.9
Amodiaquine + chloroquine	8	2.1	5	1.1	13	1.8
Amodiaquine + quinine	2	0.3	6	1.6	8	0.7
SP + artemisinins	0	0	3	0.5	3	0.2
Halofantrine	0	0	2	0.3	2	0.1
Mefloquine	0	0	2	0.3	2	0.1
No antimalarial drug prescribed	40	7.0	68	20.4	108	11.3

HC = health centre; **DH** = district hospital; **SP** = sulfadoxine-pyrimethamine

However, when correctness of treatment was additionally conditioned by the appropriate dose of the antimalarial drug (Section 2.8.1.4), the recommended treatment for uncomplicated malaria decreased from 55.1% to only 18.8%. Health workers prescribed recommended treatment less commonly in HC/DHs (9.7%, 95% CI: 5.9-13.4) than in

dispensaries (23.1%, 95% CI: 17.1-29.0). Adequate treatment was prescribed for a further 46.9% of patients and of particular concern the inappropriate treatment was prescribed for 34.3% of patients. The results on correctness of treatment based on the choice of drug and appropriateness of dosage for uncomplicated malaria according to the type of facility are presented in Table 3.14.

Table 3.14: Correctness of treatment based on the choice of drug and appropriateness of dosage for children aged 2-59 months who were brought to an outpatient facility for an initial consultation with uncomplicated malaria: results according to the type of facility

Correctness of treatment[a]	Dispensary (N=596)		HC/DH (N=444)		Total (N=1040)	
	No (%)	95% CI	No (%)	95% CI	No (%)	95% CI
Recommended	155 (23.1)	17.1, 29.0	46 (9.7)	5.9, 13.4	201 (18.8)	14.2, 23.3
Adequate	267 (46.7)	38.9, 54.5	228 (47.4)	36.9, 57.8	495 (46.9)	40.8, 53.0
Inappropriate	174 (30.2)	21.1, 39.4	170 (43.0)	30.7, 55.3	344 (34.3)	26.7, 42.0

[a] See Section 2.8.1.4 for definitions
HC = health centre; **DH** = district hospital; **CI** = confidence interval

The main reasons for deviation from the guidelines are the overdose and underdose prescriptions of SP monotherapy (Table 3.15). Among all children who had SP monotherapy prescribed, 20.8% and 47.1% had SP prescribed below and above recommended dose, respectively. Considerably more children (28.9%) were under-dosed in the 12 to 47 months age group compared to infants 3 to 11 months (12.5%) and children aged 47 to 59 months (8.1%). Amodiaquine alone or in combination with other antimalarials was prescribed for 117 children with uncomplicated malaria. Only 9 children (7.8%, 95% CI: 0.5-15.1) had amodiaquine prescribed according to the NMCP recommended dose while 76 (62.8%, 95% CI: 52.1-73.5) were underdosed and 32 (29.4%, 95% CI: 18.6-40.1) were overdosed.

Table 3.15: Distribution of recommended, underdosed and overdosed prescriptions of SP monotherapies across different child age groups

Age group	Recommended[a]			Underdosed			Overdosed		
	No	%	95% CI	No	%	95% CI	No	%	95% CI
< 3 months (N=25)	12	40.4	16.6, 64.3	1	7.6	0, 22.0	12	52.0	32.9, 71.1
3-11 months (N=170)	107	68.0	57.2, 78.9	23	12.5	5.1, 19.8	40	19.5	10.4, 28.6
12-47 months (N=313)	28	7.6	2.5, 12.7	89	28.9	18.3, 39.5	196	63.5	51.9, 75.2
47-59 months (N=71)	39	58.5	44.6, 72.4	7	8.1	1.4, 14.8	25	33.4	20.2, 46.6
Total (N=579)	186	32.2	26.6, 37.7	120	20.8	13.8, 27.7	273	47.1	39.1, 55.0

[a] See Table 2.19 for NMCP recommendations
CI = confidence interval

3.3.4.4 Treatment of severe malaria

Although the survey was not designed to recruit large numbers of children with severe malaria, there was evidence of poor adherence to the recommended treatment guidelines for severe malaria, particularly for children managed before referral for hospitalisation. Table 3.16 presents the correctness of treatment practices based on the choice of antimalarial drug for referred and admitted children with severe malaria.

Table 3.16: Correctness of treatment for children aged 2-59 months who were brought to an outpatient facility for an initial consultation with severe malaria: results according to the type of referral for hospitalisation

Correctness of treatment[a]	Referred (N=21)		Admitted (N=42)		Total (N=63)	
	No	%	No	%	No	%
Recommended	1	4.5	20	45.2	21	29.9
Adequate	11	56.7	19	46.6	30	50.4
Inappropriate	9	38.8	3	8.2	12	19.7

[a] See Section 2.8.1.4 for definitions

Children with severe malaria received 14 different antimalarial treatments. Quinine monotherapy in different formulations was prescribed to 25 (34.8%) children. However, intramuscular quinine, the recommended treatment of severe malaria before referral for

hospitalisation, was prescribed to only one referred child. It is of particular concern that 38.8% of children referred for hospitalisation did not receive any antimalarial drug. The pattern of antimalarial drug prescriptions for referred and admitted children with severe malaria is presented in Table 3.17.

Table 3.17: Antimalarial prescriptions for children aged 2-59 months who were brought to an outpatient facility for an initial consultation with severe malaria

Antimalarial prescription	Referred (N=21)		Admitted (N=42)		Total (N=63)	
	No	%	No	%	No	%
SP	8	42.7	1	1.7	9	17.2
Amodiaquine	1	6.7	7	20.1	8	15.0
Artemisinins	0	0	6	14.3	6	8.9
Quinine IV + quinine tablets	0	0	6	11.2	6	7.0
Quinine IM	1	4.5	4	10.9	5	8.5
Quinine IV	0	0	5	11.6	5	7.2
Quinine IM + quinine tablets	0	0	4	9.9	4	6.1
Quinine IV + quinine syrup	0	0	3	5.1	3	3.2
Quinine IM + quinine syrup	1	2.8	0	0	1	1.1
SP + chloroquine IM	1	4.5	0	0	1	1.7
Quinine tablets	0	0	1	2.7	1	1.7
SP + quinine IM + quinine tablets	0	0	1	1.7	1	1.1
AQ + quinine IV + quinine tablets	0	0	1	2.7	1	1.7
No antimalarial drug prescribed	9	38.8	3	8.2	12	19.7

IM = intramuscular; **IV** = intravenous; **SP** = sulfadoxine-pyrimethamine; **AQ** = amodiaquine

3.3.4.5 Counselling

The performance of counselling and communication tasks were analysed for 1163 initial consultations of patients with fever aged 2-59 months who were not referred for hospitalisation. Forty-two percent of mothers were greeted when bringing the child into the consultation room. The caretaker was told the diagnosis and asked if she or he had any questions in only 15.3% and 2.1% of the encounters, respectively. The following counselling tasks were assessed: what treatment to give and how; provision of advise on tepid sponging, extra fluids, continued breastfeeding or feeding; when to return

immediately to the health facility, when to return if fever persists and what to do in case of vomiting. These tasks were rarely done during the consultations (ranging from 1-15%). Health workers performance in completing these tasks is shown in Table 3.18.

Table 3.18: Performance of health workers in completing counselling and communication tasks

Counselling and communication tasks	N=1163 (%)	95% CI
Greeted	464 (42.0)	32.0, 52.0
Told diagnosis	182 (15.3)	10.5, 20.0
Told what treatment to give	122 (12.4)	5.1, 19.8
How to give medication	128 (14.5)	5.9, 23.1
Advised to give extra fluids	48 (5.4)	1.6, 9.1
Advised about tepid sponging	78 (8.8)	3.8, 13.8
Return immediately if child unable to drink	8 (0.8)	0, 1.6
Return immediately if child becomes sicker	85 (6.7)	2.9, 10.4
Advised to return for follow up	156 (14.8)	8.5, 21.1
Advised to return if fever persists	33 (3.0)	0.3, 5.8
Advised on any kind of follow up	230 (20.5)	13.1, 27.8
Told to continue feeding or breastfeeding	37 (3.2)	2.2, 4.3
Advised what to do in case of vomiting	22 (1.9)	0.9, 3.0
Asked if he/she has any questions	20 (2.1)	0, 4.2

CI = confidence interval

Fortunately, one of the tasks, advice on how to give drugs, was provided for the majority of children (88%) by drug dispensers. However, only 10.7% of children received their SP while at the facility, 10.2% were observed when swallowing a drug and nearly all left the facility without advice on what to do in case of vomiting (97.5%). There were no significant differences in health workers counselling practices between districts or types of facility.

3.4 Discussion

Provision of effective malaria case management encompasses not only the use of an effective drug but also the correct performance of broader clinical tasks in accordance

with evidence-based standards. To achieve adequate quality of care, the availability of antimalarial drugs, guidelines, in-service training and supervision of health workers are assumed pre-requisites. The observations from this study highlighted a number of important issues that influence delivery of appropriate malaria case management in the Kenyan context.

3.4.1 Assessment, diagnosis and counselling

In terms of assessment and diagnosis, the focus of international (Gove, 1997; WHO, 2003a) and national recommendations (MoH, 1998; 2000a) is primarily the assessment of a child's fever, either by asking for a history of fever, measuring the temperature or feeling the hotness of body; and on the consequent presumptive diagnosis of all fevers as malaria. In this study 88.1% of patients had fever assessed by performing at least one of the clinical tasks and 89.3% of febrile patients were presumptively diagnosed as malaria. Such health worker practices present an important step that guarantees prompt access of febrile children to an antimalarial treatment at the health facility level in Kenya.

However, fever is the most common symptom, voluntarily reported as the presenting complaint by 71.4% caretakers of all sick children. In other words, even without performing any of assessment tasks, health workers are spontaneously exposed to the information on the presence of fever for the majority of febrile patients. Caretakers report less frequently symptoms such as cough, diarrhoea and ear problem (54.9%, 14.6% and 2.9%, respectively), therefore the assessment tasks to find out the presence of these symptoms are equally important. However, such explorative history tasks were rarely

done (1.9-23.1%). Currently, health workers limit their assessment to the presenting complaint reported by the caretaker. Such practice is understandable since almost half of the health workers participated in vertical malaria case management training but none had attended the course on IMCI. The IMCI training is supposed to improve these deficiencies; however, it is clear that this would require a radical change from the current practice.

Health workers performance of more complex assessment tasks, important for early detection of severe malaria and other severe diseases, was generally very low. Health workers assessed anaemia in 53% of febrile children commonly by checking the conjunctiva and rarely by checking palmar pallor (5%), as recommended by the NMCP guideline, in line with recent clinical evidence (Zucker *et al.,* 1997) and proposed by IMCI guidelines. More importantly, the presence of other signs and symptoms of suspected severe malaria (respiratory distress, seizures or dehydration) were assessed in less than 10% of all febrile children. These signs and symptoms of severe disease are rarely volunteered by caretakers of sick children in Kenya (Mwenesi *et al.*, 1995) and active clinical assessment is required to establish their presence. Such omissions from clinical assessment procedures are likely to miss an important group of sick children with a poor prognosis. Equally rare, the performance of clinical tasks such as counting of breaths, observation of chest indrawing and pinching of skin, raise a concern if these signs are used to decide upon the management of a child presenting with cough/difficult breathing or diarrhoea, as recommended by IMCI and vertical ARI and CDD guidelines. Despite the lack of health workers exposure to IMCI, ARI and CDD in-service trainings

in this study, it should be noted that most of these signs and clinical assessment tasks are taught during the pre-service training but clearly not practiced during the post-training service. This is something IMCI would need to address.

The counselling of patients with fever represents the weakest part of the current clinical process. Health workers rarely provide advice, for example, when the child needs to return to facility if he or she fails to improve (7%) or if fever persists (3%). These results, in combination with inadequate assessment of previous use of drugs and determination whether a visit is initial or a follow up, raise concerns on the appropriate use of first and second-line treatments and the appropriate follow up of patients.

Poor assessment and counselling practices related to malaria case management are in accordance with the results of malaria case management surveys reported in Tanzania (Font *et al.,* 2001; Nsimba *et al.*, 2002) and Malawi (Lin & Franco, 2000). However, our study was undertaken at the time when IMCI had not been introduced within the study districts. As such deficiencies in assessment and counselling practices that compromise the provision of effective malaria case management may improve with the extension of this programme nationwide. This assumption is based upon the focus of IMCI on both assessment and counselling and the previous studies that demonstrated significant improvements following the introduction of IMCI (Simoes *et al.*, 1997; CDC, 1998; Armstrong-Schellenberg *et al.*, 2004; Gouws *et al.*, 2004).

3.4.2 Treatment practices

Three major observations in relation to the health workers treatment practices for uncomplicated malaria are worthy of comment. First, the adherence to the national treatment recommendations was very low; second, despite a low adherence to SP monotherapy an adequate treatment sufficient to cure malaria was however prescribed to the majority of patients; and third, inappropriate treatment practices insufficient to cure malaria were still unacceptably high.

Fifty five percent of children with uncomplicated malaria were prescribed drug according to national guidelines and this finding was consistent with 45-63% of the correct treatments reported from similar studies in the Central African Republic (Rowe *et al.*, 2000), Malawi (Osterholt, 2002) and Benin (Rowe *et al.*, 2003). Yet in this study, only 19% of children with uncomplicated malaria had the correct drug prescribed according to the recommended dose, the finding consistent with 25% and 24% of the dose-correct treatments for children with uncomplicated malaria reported among non-IMCI trained health workers in Tanzania (Armstrong-Schellenberg *et al.*, 2004) and Uganda (Gouws *et al.*, 2004) respectively.

The main reasons for the decrease in recommended treatment practice (from 55% to 19%) are common prescriptions of SP below (21%) and above the recommended dose (47%). SP prescriptions below recommended dose are of particular concern since they present inappropriate treatment, inadequate to cure malaria. Contrary to the common view that a single dose regimen of SP, guarantees optimal effectiveness, the results of our

study demonstrated that the high frequency of underdosed prescriptions (21%) may compromise treatment effectiveness. Furthermore, the NMCP guideline is deficient by itself. Using the weight of a child as gold standard, it has been previously demonstrated in Western Kenya, that the NMCP recommended, age-specific SP dosage tables, result in 12% of children being underdosed (< 25/1.25 mg/kg of SP) and practically non-existent overdosing (Terlouw *et al.*, 2003). The lack of information on children's weights in our study and the evaluation of SP prescriptions based on the NMCP age-specific tables may have misclassified some of the children, however, it seems reasonable to conclude that the underdosing prescriptions combined with deficient guideline recommendations increase the risk of clinical failures and more rapid progression of SP resistance.

Nevertheless, even if only 19% of children had recommended drug prescribed according to recommended dose, an adequate treatment with non-recommended but effective drug in dosages sufficient to cure malaria was prescribed for a further 47% of patients. Of the non-recommended antimalarial treatments a wide variety of medications were prescribed. Of interest, over 22% were combinations of available antimalarial drugs, and particularly notable at the level of health centres and district hospitals. This represents a shift in practice, albeit in line with an international position of combination therapy (WHO, 2001a), but at variance to current national policy at the time of the study. The major concern here is that such non-recommended drugs are of uncertain safety margin when co-administered, particularly when prescribed above recommended doses, and without any empirical evidence of additional benefits they present supplementary unnecessary cost for Kenyan Ministry of Health and patients.

Perhaps the greatest concern is that 34% of children received an inappropriate treatment that is unlikely to cure uncomplicated malaria. Apart from SP prescriptions below recommended dose, the other reasons include use of chloroquine, underdosed prescriptions of amodiaquine and artemisinins, or no antimalarial prescription at all. Currently, health workers practices at government facilities in Kenya do not guarantee an access to effective antimalarial treatment. However, while these findings demonstrate deficiencies in treatment practices in relation to guidelines and indicate sub-optimal health workers' performance it should be acknowledged that not all fevers are malaria and recommendations equating all fevers as malaria result with significant overdiagnosis as demonstrated in Section 1.4.1. Therefore, prescribing inappropriate treatments is not necessarily related to true malaria cases, however, the focus of this study and quality of care studies in general are not true malaria cases but health workers' treatment practices in accordance with standards regardless of their deficiencies.

Finally, regardless of the case definition applied to measure the recommended treatment, the indicators of the current treatment practices for uncomplicated malaria fall far below the optimistic KNMS target defined as *"80% of fevers treated at outpatient facilities according to national recommendations"* (DOMC, 2001). A significant improvement of health workers treatment practices is required if this optimistic target is to be achieved by the year 2006.

3.4.3 Health systems support

The analysis of health systems support focused on health facility and health worker characteristics necessary for adequate performance of malaria case management. SP, the recommended first-line drug for uncomplicated malaria, was available in almost all facilities. At least one of two recommended second-line drugs (amodiaquine or quinine) were available in about a half of the facilities, more commonly in health centres and district hospitals (69%) than in dispensaries (46%). Furthermore, only one-third of facilities stocked injectable quinine, the recommended treatment for severe malaria prior to referral (Table 3.7). The KNMS specifies target of "*80% of government facilities with continuous and adequate supplies of drugs essential for the management of malaria*" (DOMC, 2001). In 2001, only supply of the first-line drug met this target, however, the supplies of second-line drugs and drugs for management of severe malaria were still inadequate.

With regard to the health workers characteristics, a significant proportion attended malaria in-service training, possessed guidelines and had at least one supervision visit in the past 6 months (44.9%, 57.8% and 76.3%, respectively). Health workers at dispensaries were more exposed to training, guidelines and supervision than their colleagues in health centres and district hospitals. However, qualitative aspects of malaria in-service training and supervision visits were far less satisfactory. It is assumed that health workers exposure to these interventions would improve the quality of malaria case management. In the following Chapter these issues are discussed and the detailed

analysis of factors influencing the quality of treatment practices for uncomplicated malaria is presented.

3.5 Conclusion

This study has identified a number of deficiencies in health workers clinical practices that compromise the delivery of antimalarial treatment and thus limit the effectiveness of malaria case management. The health facility based malaria case management indicators are significantly lower compared to the optimistic KNMS targets of 80%. To curb malaria mortality in Kenya, redressing these deficiencies represents a challenge for clinical services, especially as we embark upon a new era of more expensive and complex treatment regimens, such as combination therapies.

CHAPTER 4:

Predictors of the quality of health worker treatment practices for uncomplicated malaria

4.1 Introduction

Several authors have examined the factors that influence good clinical practice and adherence to national clinical guidelines (Section 1.6.4). In this chapter the facility, health worker and patient characteristics described in Chapter 3 are examined in relation to the health workers adherence to national treatment recommendations for uncomplicated malaria using new statistical approaches for modelling multi-level data as described in section 2.13.1.2.

4.2 Methods

Detailed presentation of the methods and materials used to conduct the paediatric health facility survey is provided in Chapter 2. In the same chapter (Section 2.13.1.2) the analytic strategy of multiple binomial logistic regression is presented. In the Methods section of this chapter the definitions used for the predictors analysis of treatment quality are laid out and the detailed statistical procedures used for the multilevel modeling of each studied factor are explained.

4.2.1 Definitions

The definitions of uncomplicated malaria and correctness of treatment are presented in Section 2.8.1. Briefly, uncomplicated malaria was defined as a history of fever during the present illness (according to the study interviewers), the absence of a negative blood slide (according to the record in patient-held cards) and child treated as an outpatient (according to the observed health worker). Three categories of treatment quality were defined (recommended, minor errors, and inappropriate) and the definition of the "correctness" of antimalarial treatment was based on the choice of antimalarial drug only,

without considering the appropriateness of the dosage (Section 2.8.2.4). The inclusion of dosage would have been an additional layer of refinement that would have resulted in comparatively small, multiple outcomes and would have reduced the study's ability to statistically test broad predictors of treatment choice. Drug doses are dealt with separately as part of the descriptive analysis in Section 3.3.4.3.

4.2.2 Statistical procedures for the factors examined

In the univariate analysis, the odds ratio (OR), p-value, and 95% confidence interval (CI) for the association of each category of treatment quality (recommended, minor errors, and inappropriate) was computed with the following factors: duration of the consultation; starting time of the consultation (before 1:00 p.m. versus 1:00 p.m. or later); caseload during two days of the survey visit, both as a continuous variable and a dichotomous variable ($\geq$30 versus < 30 child consultations); child's age; caretaker's report during the consultation on previous use of SP; main complaint of fever; health worker's experience (years working as a health worker); whether the health worker attended malaria in-service training and all variables listed in Table 4.3. For supervision, the previous six months was the focal period. The quality (in three levels: no supervision, supervision with observation of a consultation and feedback, and supervision without observation and feedback) was examined and quantity (in three levels: no supervision, 1-3 visits, and 4-10 visits). Availability of SP could not be studied because SP was in stock in nearly all (97.7%) facilities. Statistical interactions were evaluated between in-service malaria training and health workers pre-service training, supervision and in-service training, in-service training and availability of malaria treatment wall charts, pre-service training and availability of second-line drugs, and availability of guidelines and in-service training.

To adjust for confounding, factors with a p-value < 0.15 from the univariate analysis and interaction terms with p-value < 0.05 were entered into three multivariate logistic regression models (as in the univariate analysis, one model for each category of treatment quality). Factors that did not initially meet the entrance criteria for the multivariate analysis (i.e. "non-significant" [$p \geq 0.15$]) were then entered into the three multivariate models, one factor at a time. If the addition of a "non-significant" variable changed the OR of any already-included variable by > 10%, the additional variable was retained in the final multivariate model.

Although meeting the entrance criteria for the multivariate analysis, variables for health facility type and caseload ≥30 were excluded because they were strongly correlated with health workers' pre-service training: clinical officers were much more likely than nurses and nursing aides to have high caseloads and to have never worked in dispensaries. Similarly, the quality of supervision variable was excluded because more frequent supervisory visits were much more likely to include supervision with clinical observations and provision of feedback and variable frequency of supervision has shown the stronger associations with treatment quality. The malaria diagnosis variable was excluded because it was believed to be in the causal pathway between other independent variables and treatment quality. The three multivariate models were forced to contain the same variables: any variable meeting the entrance criteria for one model was automatically entered into the other two models. This approach ensured that the three ORs (one from each model) for a given factor would be adjusted for the same covariates.

4.3 Results

4.3.1 Description of the sample

In 81 health facilities, 142 health workers were observed as they performed 1864 sick child consultations. Of 1864 children, 170 consultations (9.1%) were excluded because the exit interview was not performed with a caretaker (Section 3.3.1). For predictors analysis, a further 40 consultations (2.1%) were excluded since they were performed by 7 health workers for whom data were not collected (Section 3.3.1). The descriptions of the health workers and health facilities are presented in Sections 3.3.2.2 and 3.3.2.3; a summary of the key factors examined in the present analysis is presented in Table 4.1.

Table 4.1: Characteristics of health workers who treated children with uncomplicated malaria and outpatient facilities where the treatment occured

Characteristic	No	%
Health workers characteristics (N=135)		
Male sex	66	48.0
Pre-service training		
Clinical officer[a]	30	15.7
Nurse	94	76.8
Nursing aide	11	7.6
HW received in-service malaria training	59	44.9
HW has malaria guidelines	77	57.8
HW received at least one supervision visit in the past 6 months	94	76.3
Health facility characteristics (N=81)		
Health facility type		
Dispensary	48	71.3
Health centre	29	26.0
District hospital	4	2.7
Malaria treatment wall chart in the consultation room	22	27.0
SP (any formulation) in stock	80	97.7
Amodiaquine (any formulation) in stock	26	32.1
Quinine tablets in stock	18	18.1
Injectable quinine in stock	26	32.7
Chloroquine (any formulation) in stock	47	64.3
Any formulation of amodiaquine or quinine in stock	43	53.1

[a] The clinical officer category contains 3 consultations done by one physician
HW = health worker; **SP** = sulfadoxine-pyrimethamine

For the predictors analysis, 1006 sick children met the definition of uncomplicated malaria: 567 (56.9%) received recommended treatment, 314 (30.4%) had a minor error, and 125 (12.7%) were given an inappropriate treatment. Only 20 caretakers reported that their child had been treated with SP before coming to the health facility. The distribution of antimalarial treatments in each category of treatment quality is presented in Table 4.2.

Table 4.2: Distribution of antimalarial treatments in each category of treatment quality

Antimalarial treatment	Recommended (N = 567)		Minor errors (N = 314)		Inappropriate (N = 125)	
	No	%	No	%	No	%
SP	563	99.5	0	0	0	0
Amodiaquine	4	0.5	55	14.8	0	0
Quinine	0	0	36	12.2	0	0
Chloroquine	0	0	0	0	22	26.9
Chloroquine + SP	0	0	90	33.8	0	0
Chloroquine + amodiaquine	0	0	12	5.8	0	0
Amodiaquine + SP	0	0	31	6.5	0	0
Quinine + amodiaquine	0	0	8	2.5	0	0
Quinine + SP	0	0	63	20.7	0	0
Artemisinins	0	0	16	3.2	0	0
Artemisinins + SP	0	0	3	0.5	0	0
No antimalarial treatment	0	0	0	0	103	73.1

SP = sulfadoxine-pyrimethamine

4.3.2 Predictors of treatment quality

For each factor, ORs from the three models can be read together. For example, compared to children treated in consultation rooms without a malaria treatment wall chart, children treated in rooms with a wall chart were significantly more likely to receive recommended treatment (OR for recommended treatment [OR_{rec}]=1.86, 95% CI: 1.01-3.42) and significantly less likely to have a minor error (OR for a minor error [OR_{min}]=0.51, 95% CI: 0.27-0.98); no association was found with inappropriate treatment (OR for a major error [OR_{maj}]=0.99, 95% CI: 0.50-1.98) (Table 4.4).

Chloroquine availability was associated with a significantly lower likelihood of recommended treatment (OR_{rec}=0.56). Compared to children treated by unsupervised health workers, children treated by health workers supervised 4-10 times in the past 6 months were significantly less likely to receive inappropriate treatment (OR_{maj}=0.28). Infants had significantly fewer minor errors (OR_{min}=0.64). Children whose caretaker spontaneously reported fever as the main complaint were significantly more likely to receive recommended treatment (OR_{rec}=1.76) and significantly less likely to receive inappropriate treatment (OR_{maj}=0.47).

Generally, nursing aides adhered much more closely to guidelines than nurses and clinical officers, and the effect of health workers' pre-service training on treatment quality depended on the availability of second-line drugs at the facility. When second-line drugs were not in stock, children were significantly more likely to receive inappropriate treatment if treated by a clinical officer (OR_{maj}=25.45) or nurse (OR_{maj}=7.11) compared to a nursing aide (Table 4.5). When second-line drugs were in stock, children treated by clinical officers were significantly less likely to receive recommended treatment and more likely to have minor errors (OR_{rec}=0.07 and OR_{min}=13.06), and children treated by nurses were significantly less likely to receive recommended treatment and more likely to have major errors (OR_{rec}=0.09 and OR_{maj}=3.27). The effect of in-service malaria training depended on whether a health worker possessed a copy of the NMCP guideline. When health workers did not have the guideline, there was no significant association between in-service training and the quality of treatment. However, when health workers had the guideline, children seen by trained

health workers were significantly more likely to receive recommended treatment (OR_{rec}=2.98) and significantly less likely to receive inappropriate treatment (OR_{maj}=0.25).

Among factors excluded from the multivariate analysis, several interesting univariate results were found. For example, treatment quality was significantly better for children whose malaria was diagnosed by the health worker, for children treated in dispensaries, and for children treated by health workers who had a 2-day caseload <30 consultations (Table 4.3). However, as described in the Section 4.2.2, the influence of health facility type and high caseload cannot be separated from health workers' pre-service training.

Table 4.3: Univariate results for associations with treatment quality for uncomplicated malaria

Factor	No. of consul-tations	No (%) of consultations with each category of treatment quality (weighted results)			Inappropriate (major error)		Adequate (minor error)		Recommended (no error)	
		Major error	Minor error	No error	OR	p-value	OR	p-value	OR	p-value
Health facility and health worker factors										
Chloroquine in stock										
Yes	573	86 (15.3)	204 (32.7)	283 (51.9)	1.50	0.206	1.01	0.976	0.85	0.551
No	433	39 (8.4)	110 (26.5)	284 (65.1)	Ref.		Ref.		Ref.	
Second-line drugs (any formulation of amodiaquine or quinine) in stock										
Yes	580	71 (12.2)	241 (38.5)	268 (49.3)	1.07	0.848	1.78	0.073	0.56	0.033
No	426	54 (13.4)	73 (20.0)	299 (66.6)	Ref.		Ref.		Ref.	
Pre-service training										
Clinical officer[a]	253	37 (15.0)	137 (53.4)	79 (31.6)	3.38	0.052	2.19	0.317	0.30	0.081
Nurse	700	84 (12.6)	168 (25.9)	448 (61.6)	3.00	0.048	0.77	0.725	0.86	0.829
Nursing aide	53	4 (6.8)	9 (23.8)	40 (69.5)	Ref.		Ref.		Ref.	
Interaction terms between second-line drug in stock and pre-service training										
Second-line drug and clinical officer					0.07	0.026	8.35	0.119	0.45	0.480
Second-line drug and nurse					0.21	0.183	15.55	0.037	0.12	0.050
Malaria wall chart in consultation room										
Yes	276	26 (9.2)	77 (23.2)	173 (67.6)	0.82	0.540	0.62	0.128	1.61	0.099
No	730	99 (14.1)	237 (33.2)	394 (52.8)	Ref.		Ref.		Ref.	
Malaria guidelines document present										
Yes	609	69 (10.1)	161 (25.6)	379 (64.3)	0.62	0.134	0.55	0.049	2.12	0.008
No	397	56 (16.5)	153 (37.4)	188 (46.1)	Ref.		Ref.		Ref.	
Malaria in-service training										
Yes	499	52 (9.5)	127 (25.9)	320 (64.6)	0.56	0.090	0.64	0.123	1.96	0.018
No	507	73 (15.7)	187 (34.5)	247 (49.8)	Ref.		Ref.		Ref.	
Interaction term between malaria guidelines and in-service training					0.13	<0.001	0.94	0.920	2.75	0.085
Interaction term between malaria in-service training and wall chart					0.91	0.884	1.13	0.842	0.91	0.874

Table 4.3: continued. Univariate results for associations with treatment quality for uncomplicated malaria

Factor	No. of consultations	No (%) of consultations with each category of treatment quality (weighted results)			Inappropriate (major error)		Adequate (minor error)		Recommended (no error)	
		Major error	Minor error	No error	OR	p-value	OR	p-value	OR	p-value
Frequency of supervision										
4–10 visits in past 6 months	268	19 (6.5)	64 (22.5)	185 (71.0)	0.43	0.020	0.73	0.444	1.91	0.079
1–3 visits in past 6 months	430	60 (15.5)	125 (28.8)	382 (55.7)	1.01	0.983	0.67	0.240	1.48	0.201
0 visits in past 6 months	308	46 (13.8)	125 (42.5)	137 (43.7)	Ref.		Ref.		Ref.	
Interaction term between malaria in-service training and supervision					0.43	0.250	0.82	0.762	1.53	0.466
Sex of the health worker										
Male	483	66 (13.2)	165 (34.5)	252 (52.3)	1.17	0.628	1.53	0.160	0.64	0.113
Female	523	59 (12.3)	149 (26.7)	315 (61.0)	Ref.		Ref.		Ref.	
Experience working as a health worker (per additional year, ranging from 0–41)	1006	NA	NA	NA	1.00	0.971	0.96	0.031	1.03	0.023
Caseload during two day survey visit (per additional patient, ranging from 1–47)	1006	NA	NA	NA	1.00	0.810	1.00	0.816	1.00	0.929
Child or consultation factors										
Chief complaint of fever										
Yes	614	51 (8.9)	181 (27.4)	382 (63.7)	0.48	<0.001	0.87	0.252	1.58	<0.001
No	392	74 (19.1)	133 (35.4)	185 (45.6)	Ref.		Ref.		Ref.	
Child's age										
Less than 12 months	319	53 (16.7)	74 (21.8)	192 (61.5)	1.40	0.199	0.70	0.002	1.17	0.308
12 months or more	687	72 (11.0)	240 (34.1)	375 (54.9)	Ref.		Ref.		Ref.	
Mother's report of previous use of SP										
Yes	20	2 (10.9)	7 (38.8)	11 (50.3)	1.14	0.857	1.85	0.167	0.52	0.347
No	986	123 (12.8)	307 (30.3)	556 (57.0)	Ref.		Ref.		Ref.	
Start time of consultation										
1 p.m. or later	298	33 (12.4)	85 (25.2)	180 (62.4)	0.87	0.609	0.85	0.262	1.24	0.074
Before 1 p.m.	708	92 (12.9)	229 (32.5)	387 (54.6)	Ref.		Ref.		Ref.	
Consultation length (per additional minute, range 0 – 25 minutes)	1006	NA	NA	NA	0.97	0.434	1.01	0.457	1.00	0.935

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Table 4.3: continued. Univariate associations with treatment quality for uncomplicated malaria: factors meeting entrance criteria in univariate analysis but excluded from multivariate analyses due to causal pathway and collinearity

Factor and reason for exclusion	No. of consultations	No (%) of consultations with each treatment quality (weighted results)			Inappropriate (major error)		Adequate (minor error)		Recommended (no error)	
		Major error	Minor error	No error	OR	p-value	OR	p-value	OR	p-value
Thought to be in the causal pathway with chief complaint of fever										
Health worker diagnosed malaria										
Yes	830	30 (4.5)	295 (35.0)	505 (60.4)	0.05	<0.001	4.07	<0.001	2.63	<0.001
No	176	95 (51.8)	19 (8.4)	62 (39.8)	Ref.		Ref.		Ref.	
Excluded due to high correlation with other independent variable										
Health facility type[a]										
Dispensary	583	57 (11.4)	118 (23.8)	408 (64.8)	0.63	0.160	0.38	0.001	3.04	<0.001
Health centre or district hospital	423	68 (16.0)	196 (46.9)	159 (37.1)	Ref.		Ref.		Ref.	
Caseload during the 2 days of the survey[b]										
30 or more child consultations	111	24 (18.6)	52 (52.4)	35 (29.0)	1.83	0.344	1.95	0.274	0.37	0.047
Less than 30 child consultations	895	101 (12.2)	262 (28.4)	532 (59.4)	Ref.		Ref.		Ref.	
Quality of supervision[c]										
Supervision with observation and feedback	154	15 (9.4)	41 (24.8)	98 (65.8)	0.63	0.286	0.77	0.582	1.59	0.262
Supervision without observation and feedback	544	64 (13.2)	148 (27.1)	332 (59.7)	0.83	0.609	0.67	0.222	1.62	0.108
No supervisory visits	308	46 (13.8)	125 (42.5)	137 (43.7)	Ref.		Ref.		Ref.	

[a] The clinical officer category contains 3 consultations done by one physician

[b] Factor is strongly related to health worker's pre-service training: clinical officers were much more likely than nurses and nursing aides to have 30 or more consultations during the 2 days of the survey and not to work at dispensaries

[c] Factor is strongly related to the frequency of supervision: more frequent supervisory visits were much more likely to include supervision with observations and feedback

Ref. = reference level; **CI** = confidence interval

Table 4.4: Multivariate model for associations with treatment quality for uncomplicated malaria

	Inappropriate (major error)		Adequate (minor error)		Recommended (no error)	
Factor	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Health facility and health worker factors						
Malaria wall chart in consultation room						
Yes	0.99	(0.50 – 1.98)	0.51	(0.27 – 0.98)	1.86	(1.01 – 3.42)
No	Ref.		Ref.		Ref.	
Chloroquine in stock						
Yes	1.28	(0.62 – 2.64)	1.41	(0.78 – 2.52)	0.56	(0.32 – 0.97)
No	Ref.		Ref.		Ref.	
Second-line drugs (any formulation of amodiaquine or quinine) in stock						
Yes	3.36	(0.40 – 27.86)	0.08	(0.005 – 1.41)	8.81	(0.79 – 97.73)
No	Ref.		Ref.		Ref.	
Pre-service training						
Clinical officer[a]	25.45	(2.98 – 217.31)	0.87	(0.08 – 9.30)	0.29	(0.02 – 5.38)
Nurse	7.11	(1.14 – 44.55)	0.25	(0.03 – 1.81)	2.46	(0.30 – 20.24)
Nursing aide	Ref.		Ref.		Ref.	
Interaction terms between second-line drug in stock and pre-service training[b]						
Second-line drug and clinical officer	0.09	(0.01 – 0.99)	15.06	(0.55 – 414.28)	0.24	(0.01 – 6.45)
Second-line drug and nurse	0.46	(0.05 – 4.32)	32.49	(1.80 – 587.24)	0.04	(0.003 – 0.46)
Malaria guidelines document present						
Yes	1.42	(0.60 – 3.33)	0.54	(0.20 – 1.51)	1.39	(0.62 – 3.10)
No	Ref.		Ref.		Ref.	

Table 4.4: continued. Multivariate model for associations with treatment quality for uncomplicated malaria

	Inappropriate (major error)		Adequate (minor error)		Recommended (no error)	
Factor	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Malaria in-service training						
Yes	2.08	(0.96 – 4.50)	0.76	(0.31 – 1.90)	0.77	(0.37 – 1.62)
No	Ref.		Ref.		Ref.	
Interaction term between malaria guidelines and in-service training[b]	0.12	(0.03 – 0.46)	0.85	(0.22 – 3.28)	3.86	(1.24 – 11.96)
Frequency of supervision						
4–10 visits in past 6 months	0.28	(0.12 – 0.66)	1.12	(0.44 – 2.86)	1.70	(0.74 – 3.86)
1–3 visits in past 6 months	0.72	(0.35 – 1.50)	1.08	(0.48 – 2.45)	1.16	(0.58 – 2.32)
0 visits in past 6 months	Ref.		Ref.		Ref.	
Sex of the health worker						
Male	0.93	(0.44 – 1.95)	1.01	(0.55 – 1.85)	1.06	(0.62 – 1.82)
Female	Ref.		Ref.		Ref.	
Experience working as a health worker (per additional year, ranging from 0–41)	1.01	(0.96 – 1.06)	0.96	(0.93 – 1.01)	1.02	(0.99 – 1.06)
Child or consultation factors						
Chief complaint of fever						
Yes	0.47	(0.32 – 0.68)	0.86	(0.67 – 1.10)	1.76	(1.38 – 2.25)
No	Ref.		Ref.		Ref.	
Child's age						
Less than 12 months	1.44	(0.85 – 2.45)	0.64	(0.49 – 0.84)	1.21	(0.85 – 1.72)
12 months or more	Ref.		Ref.		Ref.	
Start time of consultation						
1 p.m. or later	0.94	(0.53 – 1.66)	0.80	(0.58 – 1.10)	1.33	(1.00 – 1.77)
Before 1 p.m.	Ref.		Ref.		Ref.	

[a] The clinical officer category contains 3 consultations done by one physician; [b] See Table 4.5 for interpretation of interaction terms;
Ref. = reference level; **CI** = confidence interval

Table 4.5: Association between interaction terms and categories of treatment quality for uncomplicated malaria

Factor	No. of consul-tations	% of consultations with each category of treatment quality			Inappropriate (major error)		Adequate (minor error)		Recommended (no error)	
		Major error	Minor error	No error	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Interaction between availability of second-line drugs and HW's pre-service training										
When second-line drugs not in stock										
Pre-service training										
Clinical officer[a]	38	28.5	48.4	23.1	25.45	(2.98 – 217.31)	0.87	(0.08 – 9.30)	0.29	(0.02 – 5.38)
Nurse	361	12.8	16.7	70.4	7.11	(1.14 – 44.55)	0.25	(0.03 – 1.81)	2.46	(0.30 – 20.24)
Nursing aide	27	2.5	37.5	60.0	Ref.		Ref.		Ref.	
When second-line drugs in stock										
Pre-service training										
Clinical officer[a]	215	12.0	54.5	33.5	2.27	(0.63 – 8.15)	13.06	(1.34 – 127.67)	0.07	(0.02 – 0.31)
Nurse	339	12.3	34.5	53.1	3.27	(1.03 – 10.31)	8.13	(0.94 – 70.05)	0.09	(0.02 – 0.35)
Nursing aide	26	11.0	10.0	79.0	Ref.		Ref.		Ref.	
Interaction between availability of guidelines and malaria in-service training										
When HWs were not trained										
Malaria guidelines present										
Yes	184	18.2	29.7	52.1	1.42	(0.60 – 3.33)	0.54	(0.20 – 1.51)	1.39	(0.62 – 3.10)
No	323	14.2	37.4	48.4	Ref.		Ref.		Ref.	
When HWs were trained										
Malaria guidelines present										
Yes	425	6.1	23.7	70.2	0.17	(0.07 – 0.45)	0.46	(0.20 – 1.05)	5.37	(2.71 – 10.63)
No	74	25.8	37.0	37.2	Ref.		Ref.		Ref.	
When guidelines were not present										
Malaria in-service training										
Yes	74	25.8	37.0	37.2	2.08	(0.96 – 4.50)	0.76	(0.31 – 1.90)	0.77	(0.37 – 1.62)
No	323	14.2	37.4	48.4	Ref.		Ref.		Ref.	
When guidelines were present										
Malaria in-service training										
Yes	425	6.1	23.7	70.2	0.25	(0.09 – 0.75)	0.65	(0.25 – 1.67)	2.98	(1.33 – 6.67)
No	184	18.2	29.7	52.1	Ref.		Ref.		Ref.	

[a] The clinical officer category contains 3 consultations done by one physician; **Ref.** = reference level; **HW** = health worker; **CI** = confidence interval

4.4 Discussion

In this Chapter the determinants of the quality of treatment for uncomplicated malaria were examined. A series of associations between health facility, health worker, and patient or consultation level factors, and health worker performance were investigated using rigorous analytical techniques.

The first main finding was that several commonly used interventions for improving health worker practices were significantly associated with prescribing recommended treatment: in-service training, possession of the NMCP guideline, treatment wall charts, and supervision. Regarding in-service training, other studies with a similar design have reported a variety of results, ranging from an association with better health worker performance (Naimoli, 2001) to an association with more minor errors (Osterholt, 2002) to no association with performance (Rowe *et al.*, 2000; Rowe *et al.*, 2003). The results revealed in this study found something new: specific subgroups of health workers for whom training seemed beneficial (health workers possessing the guideline) or inconsequential (those without the guideline). The association of possessing the guideline, however, must be interpreted with caution because we do not know whether the factor was causally related to health worker practices or simply a marker for another characteristic not measured in the study that was causally related (i.e. motivation). Perhaps motivated health workers were more likely to both possess the guideline and benefit from training.

Similarly, caution is needed when interpreting the association of treatment wall charts. Wall charts could be causally associated with better treatment, but also could be a marker for motivated health workers who are more likely to follow guidelines. The relationship may be more complex, however, given that one study found that wall charts were associated with treatment errors (Rowe *et al.*, 2000).

As with in-service training and wall charts, supervision has had different reported effects in different studies. These findings essentially agree with the results from Philippines, Zimbabwe and Benin (Loevinsohn *et al.*, 1995; Trap *et al.* 2001; Rowe *et al.*, 2001), while results from the Central African Republic and Malawi did not show an association with treatment quality (Rowe *et al.*, 2000; Osterholt, 2002). Unfortunately, most studies (including this one) had only limited details of the supervision, and thus it is difficult to make conclusions about the effectiveness of this common intervention.

The second main finding was that clinical officers and nurses were much less likely than nursing aides to adhere to guidelines. The results even suggested a dose-response relationship, with clinical officers less adherent than nurses, who were less adherent than nursing aides. This finding was remarkably similar to results from Benin for the treatment of fever (Rowe *et al.,* 2003) and diarrhoea (Rowe *et al.*, 2001). Furthermore, in this study, the effect of pre-service training depended on the availability of second-line drugs. Several reasons may explain these results. First, nursing aides may not know how to prescribe second-line drugs and therefore avoid using them. Second, nursing aides may be better at following clinical algorithms because they have less of a "medical vocabulary" of alternative diagnoses and treatments that might "interfere" with the

simple "fever = malaria" concept upon which the guideline is based. Third, clinical officers and, to a lesser extent, nurses, may have been taught (or socialised) that their clinical judgment can overrule guidelines. Indeed, they may view guidelines as suggestions, rather than rules that should be followed systematically. Fourth, clinical officers and nurses may have lost confidence in SP. Fifth, clinical officers and nurses may be more susceptible to pressures to prescribe second-line drugs inappropriately, such as profit motives or caretaker demands. Finally, it is possible that the causal factor is not health worker pre-service training, but rather another closely related factor such as health facility type or caseload, the effects of which could not be separated from pre-service training.

The third main finding was that child and consultation factors were significantly associated with treatment quality. First, the caretakers' report of fever as the chief complaint was associated with better treatment quality. A possible explanation is that health workers consider a fever less important if a caretaker does not mention it voluntarily. The result supports interventions that teach caretakers to actively report their child's fever. Similarly, it may be helpful to instruct health workers during training courses and supervision visits to check for fever and always pay attention to the fevers they identify because if the caretaker does not mention it, malaria may be missed.

The second child-level factor was the child's age. Infants were less likely than older children to have minor errors. Perhaps this reveals health workers' concerns that second-line drugs such as amodiaquine or quinine are less safe for younger children. If this

hypothesis is true and if failure rates with SP continue to rise, then appropriate use of second-line drugs should be emphasised for infants. A third factor, which was a consultation characteristic, only had borderline significance; however, our results suggested that children seen after 1 p.m. received better treatment. A possible explanation is that health workers are less rushed in the afternoon, as most patients arrive at facilities in the morning. If confirmed, the results support interventions to space out consultations more evenly throughout the day or adding extra staff only for the mornings.

The last main finding was that two statistical interactions were identified. Although interactions complicate the interpretation of results (especially with three models), they act as a high-resolution lens for examining the influences of health worker performance. Intuitively, interactions, which allow the effect of a factor to be conditional on other factors, seem to be an appropriate element of models that explain a phenomenon as complex as health worker performance.

4.5 Conclusions

With all necessary caution in the interpretation of the results and methodological limitations encountered (Section 2.14), the study results indicated that programmatic interventions such as in-service malaria training, provision of guidelines and wall charts, and more frequent supervision were associated with better treatment quality. However, neither in-service training nor possession of the guideline showed an effect by itself. Conversely, availability of chloroquine and higher health workers' pre-service training were associated with more treatment errors. Child and consultation factors such as the

main complaint of fever, younger age and consultation in afternoon hours were also associated with better treatment quality. The results of this study indicated various determinants of health workers performance that require further validation in the prospective, interventional trials.

CHAPTER 5

Accuracy of malaria diagnosis, quality of clinical assessment and ability of clinical signs and symptoms to predict malaria in older children and adults

5.1 Introduction

People living in malaria endemic areas are infected repeatedly, and they acquire functional immunity to the clinical consequences of malaria infection as they get older. As presented in Section 1.3.5, in areas of high intensity transmission, children usually develop a functional immune response by school age, as demonstrated by the massive decline in incidence of malaria disease by this age. Furthermore, severe malaria and malaria death are rare events in older children and adults. This pattern of age-specific acquisition of functional immunity is shifted to older age groups as transmission intensity, measured by the frequency of parasitic exposure, decreases.

In most rural health facilities in Africa, laboratory support to diagnose malaria is not available and diagnosis is based on clinical signs and symptoms. However, few studies have investigated the clinical predictors of malaria among older children and adults in Africa compared to similar studies of clinical predictors in young children (Section 1.4.2).

Fever usually represents an entry point for malaria case management recommendations, but unlike in children below 5 years of age, where various guidelines are in agreement on how to manage fever, and provide explicit recommendations for fever management in different malaria endemic settings, case management recommendations for older children and adults are commonly unclear and rarely harmonised (Section 1.5.2.1). However, it appears that in this age group most of the guidelines recognise the importance of

identifying other causes of fever, yet none of them clearly state how this criterion should be used and what signs and symptoms present an alternative explanation of fever.

Despite our understanding of the age-structured risks of clinical malaria and case management recommendations suggesting the search for other causes of fever, older children and adults appear more likely to be diagnosed as having malaria than young children at outpatient facilities. The examination of outpatient registers from four Kenyan districts of different malaria endemicities revealed that a significant proportion (district range: 43-49%) of all malaria diagnoses are made among populations above 14 years of age and there was no important difference observed between the districts of different malaria endemicities (Sections 2.3.1.3, 2.3.2.3, 2.3.3.3 and 2.3.4.3). The frequency with which "malaria" is diagnosed as a cause of outpatient attendance is hard to reconcile with our understanding of the clinical epidemiology of malaria (Section 1.3.5). One explanation for frequent malaria diagnoses in older children and adults may be that malaria diagnosis is simply convenient, requiring no search for other causes of fever. However, observational studies investigating the quality of fever assessment and clinical evaluation to exclude malaria in febrile older children and adults have not been undertaken in tropical Africa.

This chapter will focus on: 1) the accuracy of the routine clinical diagnosis of malaria; 2) a description of current health workers practices in the clinical assessment of febrile patients; and 3) the ability of clinical signs and symptoms to predict malaria infection in febrile older children and adults.

5.2 Methods

Detailed presentation of the materials and methods applied in the older children and adult survey are presented in the following sections of the Chapter 2:

1) Characteristics of the study districts (Section 2.3)
2) Development of the sampling frame (Section 2.6.2)
3) Sampling procedures (Section 2.7.2)
4) National guidelines and study case definitions (Section 2.8.2)
5) Data collection forms (Section 2.9.2)
6) Survey teams and training of surveyors (Section 2.10.2)
7) Survey procedures (Section 2.11.2)
8) Statistical analysis (Section 2.13.2)

Briefly, the survey among older children and adults was a cross-sectional, cluster sample health facility survey, stratified according to the availability of functional malaria microscopy, and conducted in two districts: Kwale, a hyperendemic area on the Coast, and Kisii, mesoendemic area in the Western highlands. Data collection included direct observation of the routine outpatient consultations, exit examination of the observed patients by study physicians, health worker interview with the observed clinician and preparation of blood smear in febrile patients for the post-survey reading. The results on the use and interpretation of microscopy, and the accuracy of the routine reading of malaria slides are separately presented in Chapter 6.

5.3 Results

5.3.1 Description of the sample

The survey included 1292 direct observations of outpatient consultations for patients above 5 years of age that were managed by 76 health workers at 46 government health facilities in the two districts. Exit examination could not be performed for 34 patients (2.6%) and these observations were excluded from the analysis. Of 1258 analysed consultations, 830 were undertaken at 29 facilities without microscopy, and 428 were performed at 17 facilities with functional microscopy. Health worker interview was performed for all observed health workers (76). The distribution of the surveyed health facilities, health workers and patients' consultations across two districts and two types of facility are presented in Table 5.1.

Table 5.1: Distribution of the surveyed health facilities, health workers and patients' consultations across two districts and two types of facility

District	**HFs with microscopy**	**HFs without microscopy**	**All health facilities**
KWALE			
Health facilities	10	15	25
Health workers	17	21	38
Consultations	218	412	636
KISII			
Health facilities	7	14	21
Health workers	14	24	38
Consultations	210	418	622
TOTAL			
Health facilities	17	29	46
Health workers	31	45	76
Consultations	428	830	1258

HF = health facility

5.3.2 Characteristics of health workers

The mean age of the participating health workers was 37 years (range: 25-53 years). The average health workers professional experience and the time period spent in the surveyed

facility were 13 years (range: 2-29 years), and 4 years and 6 months (range: 1 month-20 years), respectively. The majority of observed health workers were nurses (77.6%), followed by clinical officers (19.7%) and nursing aides (2.6%). Almost half (48.7%) of health workers were in charge of the surveyed facilities. Fifty-three percent of health workers had attended in-service malaria training and possessed a NMCP malaria guideline, more commonly in Kisii district (84.2%) than in Kwale district (21.1%). Health workers characteristics across two districts are presented in Table 5.2.

Table 5.2: Health workers demographics, exposure to in-service training, guidelines and supervision across two districts

Health workers characteristics	**KWALE**	**KISII**	**TOTAL**
	N=38 (%)	**N=38 (%)**	**N=76 (%)**
Male sex	25 (65.8)	16 (42.1)	41 (53.9)
In-charge of health facility	19 (50.0)	18 (47.3)	37 (48.7)
Pre-service training			
Clinical officer	10 (26.3)	5 (13.2)	15 (19.7)
Registered nurse	1 (2.6)	5 (13.2)	6 (7.9)
Enrolled nurse	25 (65.8)	28 (73.7)	53 (69.7)
Nursing aide	2 (5.3)	0	2 (2.6)
HW received in-service malaria training	8 (21.1)	32 (84.2)	40 (52.6)
HW has NMCP guidelines	8 (21.1)	32 (84.2)	40 (52.6)
HW had a supervision visit in the last 6 months	29 (76.3)	38 (100)	67 (88.2)

HW = health worker

5.3.3 Characteristics of patients

5.3.3.1 Age distribution of patients

Among 1258 enrolled patients above 5 years of age, 290 (23.1%) were older children between 5 and 14 years of age, and 968 (76.9%) were adults above 14 years of age. It appeared that the proportion of older children was slightly higher in Kisii than in Kwale district (24.7% vs. 21.4%); however, the difference was not statistically significant (95% CI in Kisii=21.0-28.5 vs. 95% CI in Kwale=17.5-25.3). In adults, no difference in age

distribution was demonstrated between two districts. The age distribution of enrolled patients across districts is presented in Table 5.3.

Table 5.3: Age distribution of enrolled patients across districts

Age groups (years)	KWALE	KISII	TOTAL
	N=636 (%)	N=622 (%)	N=1258 (%)
5-9	73 (11.5)	85 (13.7)	158 (12.6)
10-14	63 (9.9)	69 (11.1)	132 (10.5)
15-24	185 (29.1)	163 (26.2)	348 (27.7)
25-34	108 (17.0)	102 (16.4)	210 (16.7)
35-44	88 (13.8)	86 (13.8)	174 (13.8)
> 44	119 (18.7)	118 (18.8)	236 (18.8)

5.3.3.2 Distribution of fevers

Patients were considered to have fever if during the exit examination a history of fever was reported in the last 48 hours or axillary temperature was ≥37.5°C (Section 2.8.3.1). Overall, the majority of patients presented with fever (80.5%). However, fever was less commonly reported as the main complaint (40.8%), and only 20.8% patients had a temperature ≥37.5°C with mean and median values of 37.0°C and 36.8°C respectively. Generally, no significant differences were observed in overall frequencies of fevers between districts apart from the observation that more patients had a raised axillary temperature in Kisii (26.7%) compared to Kwale district (14.9%).

In both districts, significant differences were observed between age groups. Overall, frequencies of all types of fever were significantly higher in older children than in adults, and age-specific differences in frequencies of fever were more obvious in Kisii than in Kwale district. For example, in Kisii district, fever was spontaneously reported in 58.4% older children compared to 28.9% adults, and raised axillary temperature was nearly 3-

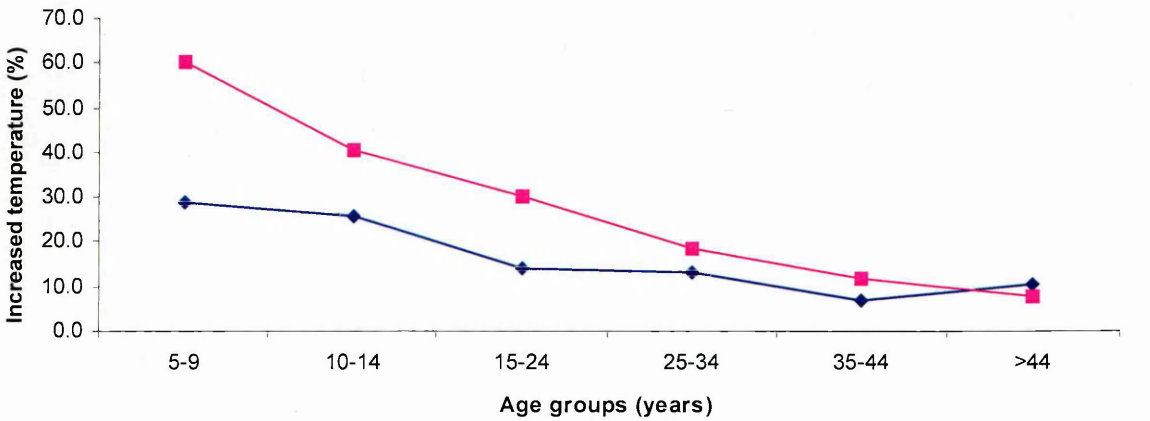
fold more common in older children than in adults (51.3% vs. 18.6%). The distribution of fevers between districts and age groups is presented in Table 5.4 and Figure 5.1.

Table 5.4: Distribution of fevers across districts and age groups

District	5-14 years		≥ 15 years		TOTAL	
	No (%)	95% CI	No (%)	95% CI	No (%)	95% CI
KWALE	N=136		N=500		N=636	
Fever[a]	110 (80.9)	73.8, 88.0	384 (76.8)	72.0, 81.6	494 (77.7)	73.3, 82.0
History of fever[b]	109 (80.2)	72.8, 87.5	377 (75.4)	70.3, 80.5	486 (76.4)	71.8, 81.0
Fever MC[c]	80 (58.8)	50.6, 67.0	208 (41.6)	34.4, 48.8	288 (45.3)	38.4, 52.1
T ≥ 37.5°C[d]	37 (27.2)	15.5, 38.8	58 (11.6)	7.7, 15.5	95 (14.9)	10.6, 19.3
KISII	N=154		N=468		N=622	
Fever[a]	143 (92.9)	89.0, 96.7	376 (80.3)	75.3, 85.4	519 (83.4)	79.1, 87.8
History of fever[b]	141 (91.6)	87.5, 95.6	366 (78.2)	73.5, 82.9	507 (81.5)	77.3, 85.8
Fever MC[c]	90 (58.4)	50.5, 66.4	135 (28.9)	22.7, 35.0	225 (36.2)	29.9, 42.4
T ≥ 37.5°C[d]	79 (51.3)	45.1, 57.5	87 (18.6)	13.7, 23.5	166 (26.7)	22.2, 31.2
TOTAL	N=290		N=968		N=1258	
Fever[a]	253 (87.2)	82.7, 91.8	760 (78.5)	75.1, 82.0	1013 (80.5)	77.3, 83.8
History of fever[b]	250 (86.2)	80.4, 91.0	743 (76.8)	73.3, 80.2	993 (78.9)	75.7, 82.2
Fever MC[c]	170 (58.6)	53.2, 64.1	343 (35.4)	30.6, 40.2	513 (40.8)	36.3, 45.2
T ≥ 37.5°C[d]	116 (40.0)	32.3, 47.7	145 (15.0)	11.7, 18.3	261 (20.8)	17.0, 24.5

[a] Reported history of fever in last 48 hours or axillary temperature ≥ 37.5°C on survey day
[b] Reported history of fever in last 48 hours (spontaneously or prompted)
[c] Fever spontaneously reported as main complaint (MC) without prompting
[d] Axillary temperature (T) ≥ 37.5°C on survey day
MC = main complaint; **T** = temperature; **CI** = confidence interval

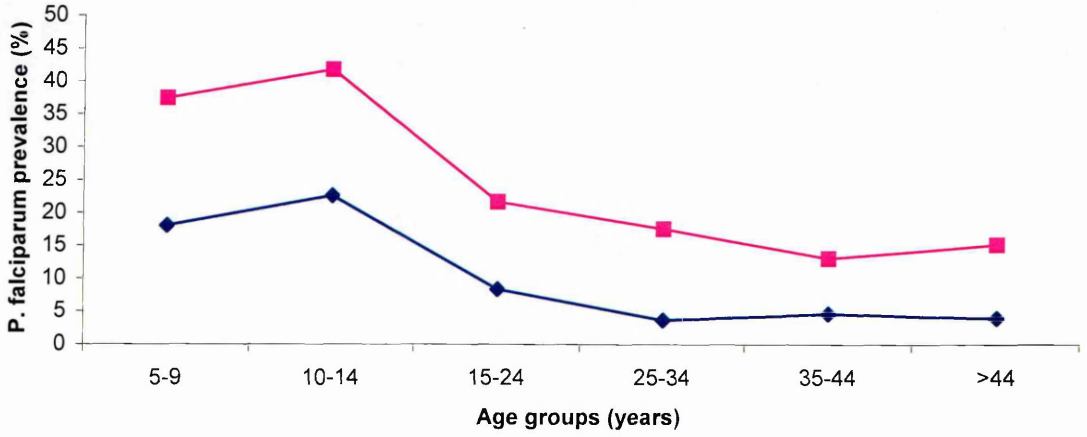
Figure 5.1: Distribution of increased axillary temperatures ≥ 37.5°C across two districts and six age groups. Pink line represents Kisii and the blue line Kwale district.



5.3.3.3 Parasite prevalence among patients with fever

Malaria blood smears were examined for 1013 patients presenting with fever (Section 2.11.2). Overall there were 179 (17.7%, 95% CI: 13.6-21.7) parasitaemic patients across two districts: 123 (23.7%, 95% CI: 18.7-28.7) in Kisii district and significantly less, 56 (11.3%, 95% CI: 7.2-15.5) in Kwale district. The majority of infections were due to *P. falciparum* (165 or 92.2%), followed by 11 *P. malariae* infections (6.2%) and two *P. ovale* infections (1.1%). There was only one case of mixed *P. falciparum* and *P. malariae* infection. All *P. malariae* infections were reported from Kwale district. Overall for two districts, older children aged 5-14 years had a higher *P. falciparum* prevalence rate (30.8%, 95% CI: 23.6-38.1) than adults above 14 years (11.4%, 95% CI: 7.7-15.2). In both age groups, prevalence rates were higher in Kisii (PR_{5-14}=39.2%, 95% CI: 30.4-47.9 and $PR_{>14}$=17.6%, 95% CI: 12.4-22.7) than in Kwale district (PR_{5-14}=20.0%, 95% CI: 11.8-28.2 and $PR_{>14}$=5.5%, 95% CI: 2.5-8.4). Figure 5.2 presents *P. falciparum* prevalence rates among febrile patients across two study districts and six age groups.

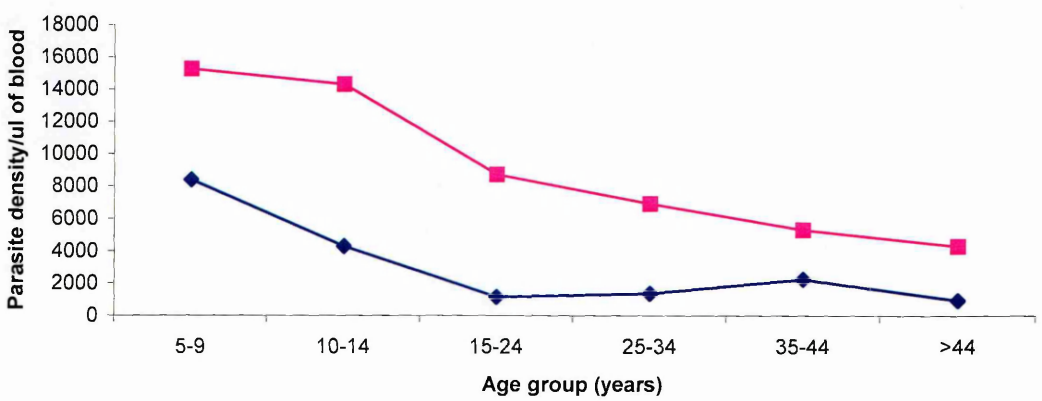
Figure 5.2: *P. falciparum* prevalence rates among febrile patients across two districts and six age groups. Pink line represents Kisii and the blue line Kwale district.



5.3.3.4 *P. falciparum* geometric mean parasite density

Among all age groups the geometric mean parasite density among *P. falciparum* positive cases was 10,061 parasites/µl (95% CI: 7,514–13,470) in Kisii district, significantly higher than 2,793 parasites/µl (95% CI: 1,556-5,011) in Kwale district. Age-specific (older children 5-14 years vs adults above 14 years) parasite densities were also higher in Kisii than in Kwale district, however, this difference was not statistically significant in older children age group. Furthermore, in each study district parasite densities were higher in older children than in adults, however, the difference was not statistically significant in Kisii district. In Kwale district, geometric mean parasite density in older children was 6,047 parasites/µl (95% CI: 2,610-14,011) compared to 1,245 parasites/µl (95% CI: 606-2,560) in adults, while in Kisii district, parasite density in older children was 14,814 parasites/µl (95% CI: 9,911-22,143) compared to 6,983 parasites/µl (95% CI: 4,636-10,519) in adults. Figure 5.3 presents *P. falciparum* geometric mean parasite densities across two study districts and six age groups.

Figure 5.3: *P. falciparum* geometric mean parasite densities across two districts and age groups. Pink line represents Kisii and the blue line Kwale district



5.3.3.5 Frequency of the most common signs and symptoms

Table 5.5 presents the distribution of the 26 most common (frequencies >5%) signs and symptoms among patients with fever. In both districts, the majority of febrile patients presented with symptoms commonly related to malaria such as headache (78.5%), chills (68.5%) and joint pains (57.7%). There was no statistically significant difference in frequencies of the most common malaria related symptoms between the two districts. Other malaria related signs and symptoms were less common but varied more between districts. They were the following: general body weakness (47.5%), shivering (26.4%), backache (16.0%), general body ache (7.1%), anaemia (6.1) and splenomegaly (4.9%).

The most common signs and symptoms possibly indicative of causes of fever other than malaria were abdominal pain (43.2%), inflamed throat (36.8%), chest pain (28.8%), running nose (24.8%) and enlarged lymph nodes (11.2%). Signs and symptoms commonly related to respiratory diseases were significantly more frequent in Kwale than Kisii district: cough (49.9% vs. 36.6%), inflamed throat (64.0% vs. 11.0%), chest pain (43.1% vs. 15.2%), running nose (36.8% vs. 13.3%), throat pain (30.6% vs. 8.5%), difficult breathing (10.3% vs. 3.1%) and abnormal chest sound (7.3% vs. 2.9%). There was no significant differences in the frequencies of various fever characteristics across districts compared to all patients sample presented in Section 5.3.3.2.

Table 5.5: Distribution of most common signs and symptoms among febrile patients across study districts

Signs and symptoms[a]	KWALE (N=494)		KISII (N=519)		TOTAL (N=1013)	
	No	%	No	%	No	%
Headache	391	79.2	404	77.8	795	78.5
Chills	340	68.8	354	68.2	694	68.5
Joint pain	291	58.9	293	56.5	584	57.7
Fever main complaint[b]	288	58.3	224	43.2	513	50.6
Genaral body weakness[b]	308	62.4	173	33.3	481	47.5
Cough[b]	246	49.9	190	36.6	451	44.5
Abdominal pain	219	44.3	219	42.2	438	43.2
Inflamed throat[b]	316	64.0	57	11.0	373	36.8
Fever more than 7 days	168	34.0	142	27.4	310	30.6
Chest pain[b]	213	43.1	79	15.2	292	28.8
Shivering[b]	173	35.0	94	18.1	267	26.4
Temperature ≥37.5°C[b]	95	19.2	166	32.0	261	25.8
Nausea[b]	180	36.4	76	14.8	262	25.9
Running nose[b]	182	36.8	69	13.3	251	24.8
Vomiting[b]	67	13.6	138	26.6	205	20.2
Throat pain[b]	151	30.6	44	8.5	195	19.3
Back ache[b]	60	12.2	102	19.7	162	16.0
Dizziness[b]	32	6.5	86	16.6	118	11.7
Enlarged lymph nodes[b]	107	21.7	6	1.2	113	11.2
Diarrhoea	39	7.9	59	10.0	91	9.0
Skin manifestations	38	7.7	52	10.0	90	8.9
Genearal body ache	38	7.7	34	6.6	72	7.1
Difficult breathing[b]	51	10.3	16	3.1	67	6.6
Pallor[b]	55	11.2	6	1.2	61	6.1
Abnormal chest sound[b]	36	7.3	15	2.9	51	5.0
Enlarged spleen[b]	8	1.6	42	8.1	50	4.9
Constipation[b]	41	8.3	8	1.5	49	4.8

[a] Signs and symptoms with frequencies greater than 5 % in any of two districts are reported
[b] Statistically significant difference between districts (at 5% level of significance)

Age-specific analysis of the same group of patients revealed that in both districts the following signs and symptoms were more common in febrile patients aged 5-14 years than in adults above 14 years of age: cough (61.7% vs. 36.9%), running nose (38.3% vs 20.3%), vomiting (31.6% vs. 16.5%), skin manifestations (17.4% vs. 6.1%) and enlarged spleen (11.5% vs 2.8%). The following symptoms were more frequent in adults: joint

pain (66.6% vs. 30.8%), chest pain (33.2% vs. 15.8%), backache (20.4% vs. 2.8%) and general body ache (9.2% vs. 0.8%). For some of the most common symptoms such as headache, chills, general body weakness and abdominal pain, there was no significant difference demonstrated between age groups within the study district nor between age groups overall. There was no significant difference in the frequencies of various fever characteristics between age groups compared to all patients sample presented in Section 5.3.3.2. Table 5.6 presents age-specific frequencies of the most common signs and symptoms among febrile patients across study districts.

Table 5.6: Distribution of most common signs and symptoms among febrile patients across age groups and study districts

Signs and symptoms[a]	KWALE		KISII		TOTAL	
	5-14 yrs	≥15 yrs	5-14 yrs	≥15 yrs	5-14 yrs	≥15 yrs
	N=110	N=384	N=143	N=376	N=253	N=760
	No (%)	No (%)	No (%)	No (%)	No (%)	No (%)
Headache	84 (76.4)	307 (80.0)	112 (78.3)	292 (77.7)	196 (77.5)	599 (78.8)
Chills	70 (63.6)	270 (70.3)	99 (69.2)	255 (67.8)	169 (66.8)	525 (69.1)
Joint pain[b]	35 (31.8)	256 (66.7)	43 (30.1)	250 (66.5)	78 (30.8)	506 (66.6)
Fever main complaint[b]	80 (72.7)	78 (30.8)	90 (62.9)	15 (35.9)	170 (67.2)	343 (45.1)
Body weakness	57 (51.8)	251 (65.4)	40 (28.0)	133 (35.4)	97 (38.3)	384 (50.5)
Cough[b]	73 (66.4)	173 (45.2)	83 (58.0)	107 (28.5)	156 (61.7)	280 (36.9)
Abdominal pain	45 (40.9)	174 (45.3)	63 (44.1)	156 (41.5)	108 (42.7)	330 (43.4)
Inflamed throat	61 (55.5)	255 (66.4)	22 (15.4)	35 (9.3)	83 (32.8)	290 (38.2)
Fever more than 7 days[b]	28 (25.5)	140 (36.5)	15 (10.5)	127 (33.8)	43 (17.0)	267 (35.1)
Chest pain[b]	31 (28.2)	182 (47.4)	9 (6.3)	70 (18.6)	40 (15.8)	252 (33.2)
Shivering	45 (40.9)	128 (33.3)	29 (20.3)	65 (17.3)	74 (29.3)	193 (25.4)
Temperature ≥37.5°C[b]	37 (33.6)	60 (15.6)	79 (55.2)	90 (23.9)	116 (45.9)	150 (19.7)
Nausea	29 (26.4)	151 (39.3)	19 (13.6)	57 (15.3)	48 (19.2)	208 (27.5)
Running nose[b]	57 (51.8)	125 (32.6)	40 (28.0)	29 (7.7)	97 (38.3)	154 (20.3)
Vomiting[b]	29 (26.4)	38 (9.9)	51 (35.7)	87 (23.1)	80 (31.6)	125 (16.5)
Throat pain	35 (31.8)	116 (30.2)	10 (7.0)	34 (9.0)	45 (17.8)	150 (19.7)
Back ache[b]	2 (1.8)	58 (15.1)	5 (3.5)	97 (25.8)	7 (2.8)	155 (20.4)
Dizziness	2 (1.8)	30 (7.8)	17 (11.9)	69 (18.4)	19 (7.5)	99 (13.0)
Enlarged lymph nodes	43 (39.1)	64 (16.7)	2 (1.4)	4 (1.1)	45 (17.8)	68 (9.0)
Diarrhoea	7 (6.4)	32 (8.3)	20 (14.0)	32 (8.5)	27 (10.7)	64 (8.4)
Skin manifestations[b]	15 (13.6)	23 (6.0)	29 (20.3)	23 (6.1)	44 (17.4)	46 (6.1)
General body ache[b]	0	38 (9.9)	2 (1.4)	32 (8.5)	2 (0.8)	70 (9.2)
Difficult breathing	7 (6.4)	44 (11.5)	4 (2.8)	12 (3.2)	11 (4.4)	56 (7.4)
Pallor	10 (9.2)	45 (11.8)	4 (2.8)	2 (0.6)	14 (5.6)	47 (6.3)
Abnormal chest sound	12 (10.9)	24 (6.3)	5 (3.5)	10 (2.7)	17 (6.7)	34 (4.5)
Enlarged spleen[b]	6 (5.5)	2 (0.5)	23 (16.1)	19 (5.1)	29 (11.5)	21 (2.8)
Constipation	8 (7.3)	33 (8.6)	1 (0.7)	7 (1.9)	9 (3.6)	40 (5.3)

[a] Signs and symptoms with frequencies greater than 5 % in any of age groups are included in the table
[b] Statistically significant difference (at 5% level of significance) between age groups within a district and between age groups for two districts together

5.3.4 Accuracy of clinical malaria diagnosis

Among 1258 outpatients from both districts malaria diagnosis was routinely made for 1007 (80.0%, 95% CI: 73.5-86.6) patients. There was no significant difference in the frequency of malaria diagnosis between health facilities without functional microscopy

(83.9%, 95% CI: 76.6-91.1) and facilities with microscopy (72.7%, 95% CI: 60.8-84.5). Chapter 6 presents results on the effects of microscopy on malaria case management practices from health facilities with functional microscopy. In this section the results on the accuracy of the routine clinical malaria diagnosis at facilities without functional microscopy are presented in relation to the presence of fever, across two study districts and two age groups (older children 5-14 years and adults above 14 years of age).

The majority of febrile patients (88.2%) were clinically diagnosed as malaria, this practice being significantly more common in Kisii (96.2%, 95% CI: 93.6-98.7) than in Kwale district (80.1%, 95% CI: 69.7-90.4). This was also true in both age groups (96.7% in Kisii vs 83.1% in Kwale among 5-14 years, and 95.9% in Kisii vs 79.0% in Kwale in adults), however the difference was not statistically significant in the older children's age group (Table 5.7). Furthermore, among 161 patients without fever, malaria was diagnosed in 106 (65.8%, 95% CI: 53.5-78.2) patients, more commonly in Kisii (91.9%, 95% CI: 85.8-98.0) than in Kwale district (43.7%, 95% CI: 32.2-52.2). Within each district the frequency of malaria diagnoses were similar between two age groups and no significant differences were revealed. Malaria diagnosing practices for febrile patients across two study districts and two age groups are presented in Table 5.7.

Table 5.7: Frequency of malaria diagnosis among febrile patients across districts and age groups

District	5-14 years			≥15 years			TOTAL		
	No	**%**	**95% CI**	**No**	**%**	**95% CI**	**No**	**%**	**95% CI**
KWALE	N=83			N=248			N=331		
Malaria diagnosed	69	83.1	68.5, 97.7	196	79.0	69.1, 88.9	265	80.1	69.7, 90.4
KISII	N=92			N=246			N=338		
Malaria diagnosed	89	96.7	91.6, 100	236	95.9	92.4, 99.4	325	96.2	93.6, 98.7
TOTAL	N=175			N=494			N=669		
Malaria diagnosed	158	90.3	82.0, 98.6	432	87.5	81.6, 93.3	590	88.2	82.1, 94.3

The accuracy of the routine clinical malaria diagnosis among patients with fever was compared with results of the study malaria smear using any parasitaemia as a conservative gold standard (Section 2.8.3.1). In both districts and across all age groups, the clinical diagnosis of malaria was characterised with high sensitivities (range: 84.2-100%) and negative predictive values (range: 85.7-100%), and low specificities (range: 3.7-21.4%) and positive predictive values (range: 8.2-41.6%). Apart from lower specificities in Kisii (range: 3.7-5.0%) compared to Kwale district (range: 19.7-21.4%), none of the other measures of accuracy showed statistically significant differences between districts or between age groups within the same district. Results on the accuracy of clinical malaria diagnosis across districts and age groups are presented in Table 5.8.

Table 5.8: Accuracy of clinical malaria diagnosis across districts and age groups

District	5-14 years			≥15 years			TOTAL		
	No/N	**%**	**95% CI**	**No/N**	**%**	**95% CI**	**No/N**	**%**	**95% CI**
KWALE									
Sensitivity	20/22	90.9	70.7, 100	16/19	84.2	70.7, 97.8	36/41	87.8	76.7, 98.9
Specificity	12/61	19.7	5.2, 34.1	49/229	21.4	10.8, 32.0	61/290	21.0	10.2, 31.8
PPV	20/69	29.0	12.4, 45.6	16/196	8.2	2.2, 14.1	36/265	13.6	6.3, 20.9
NPV	12/14	85.7	63.4, 100	49/52	94.2	88.1, 100	61/66	92.4	87.9, 96.9
KISII									
Sensitivity	37/38	97.4	93.0, 100	47/47	100	NA	84/85	98.8	96.7, 100
Specificity	2/54	3.7	0, 12.3	10/199	5.0	0.8, 9.3	12/253	4.7	1.2, 8.3
PPV	37/89	41.6	30.1, 53.1	47/236	19.9	12.2, 27.7	84/325	25.8	19.2, 32.5
NPV	2/3	66.7	NA	10/10	100	NA	12/13	92.3	71.7, 100
TOTAL									
Sensitivity	57/60	95.0	87.8, 100	63/66	95.5	90.0, 100	120/126	95.2	91.0, 99.5
Specificity	14/115	12.2	2.6, 21.7	59/428	13.8	7.5, 20.1	73/543	13.4	6.9, 19.9
PPV	57/158	36.1	26.1, 46.0	63/432	14.6	8.9, 20.3	120/590	20.3	14.5, 26.2
NPV	14/17	82.4	62.8, 100	59/62	95.2	90.1, 100	73/79	92.4	87.9, 96.9

PPV = positive predictive value; **NPV** = negative predictive value; **NA** = not applicable

5.3.5 Characteristics of the clinical assessment

Health workers practices in performing various assessment tasks were described to evaluate the quality of clinical assessment for patients with fever. A particular focus was on the ability of health workers to clinically assess patients to determine alternative causes of fever.

5.3.5.1 Characteristics of the clinical assessment across study districts

Only 4 of 30 indicators (Table 5.9) selected to define the quality of clinical assessment were performed for the majority of febrile patients and they were the following: determination of patient's age (94.2%), assessment of fever (74.8%), assessment of headache (60.5%) and inquiry on the previous use of drugs (55.2%). Performance of specific clinical tasks was sub-optimal in both districts. Particularly poor results were evident in the assessment of signs and symptoms that are commonly related to other causes of fever (range for 14 indicators: 0.6-39.5%). Overall, it appeared that health workers showed better performance in considering alternative causes of fever in Kwale than in Kisii district. Clinical tasks related to respiratory diseases such as the assessment of cough (47.2% vs. 32.2%), difficult breathing (7.5% vs. 3.3%), chest pain (29.6% vs. 15.0%), running nose (10.3% vs. 3.5%) and chest auscultation (23.0% vs. 7.8%) were more frequently performed in Kwale district. However, these differences could be explained by the higher frequency of respiratory symptoms in Kwale district resulting with higher rates of patients spontaneously reporting these complaints (Table 5.5), since a health workers' exposure to spontaneously reported symptom was credited as if an assessment task was performed. Clinical assessment practices for patients with fever across two study districts are presented in Table 5.9.

Table 5.9: Clinical assessment practices for patients with fever across two study districts

Health worker determined[a]	KWALE (N=494)		KISII (N=519)		TOTAL (N=1013)	
	No (%)	95% CI	No (%)	95% CI	No (%)	95% CI
General tasks						
Age	425 (90.2)	84.3, 96.2	503 (97.9)	96.3, 99.4	928 (94.2)	91.0, 97.4
Weight	6 (1.3)	0.2, 2.3	22 (4.3)	1.4, 7.2	28 (2.9)	1.3, 4.4
Temperature	118 (24.4)	12.8, 36.1	145 (28.2)	15.2, 41.1	263 (26.4)	17.8, 34.9
Initial or follow up visit	19 (4.0)	0.7, 7.3	240 (47.0)	31.7, 62.2	259 (26.2)	16.2, 36.2
Previous use of drugs	215 (44.1)	35.3, 52.8	340 (65.8)	57.1, 74.5	555 (55.2)	48.0, 62.4
Tasks related to common signs & symptoms of malaria						
History of fever	311 (63.0)	56.3, 69.6	404 (77.8)	69.4, 86.3	715 (70.6)	64.2, 77.0
Fever assessed[b]	339 (68.6)	60.8, 76.5	419 (80.7)	72.8, 88.6	758 (74.8)	68.6, 81.1
Duration of fever	83 (16.9)	10.4, 23.4	360 (69.6)	60.3, 79.0	443 (44.0)	31.7, 56.2
Chills	103 (20.9)	14.5, 27.2	197 (38.0)	30.7, 45.2	300 (29.6)	23.8, 35.4
Shivering	18 (3.6)	1.7, 5.5	27 (5.2)	2.8, 7.6	45 (4.4)	3.0, 5.9
Headache	255 (51.6)	44.0, 59.2	358 (69.0)	63.8, 74.1	613 (60.5)	55.7, 65.3
Joint pain	136 (27.5)	22.1, 32.9	188 (36.2)	31.6, 40.8	324 (32.0)	28.3, 35.7
Conjunctival pallor	223 (46.3)	34.9, 57.6	267 (51.6)	37.3, 66.0	490 (49.1)	40.0, 58.1
Palmar pallor	5 (1.0)	0, 2.0	68 (13.2)	4.2, 22.2	73 (7.3)	2.2, 12.3
Pallor assessed[c]	225 (45.6)	34.8, 56.3	275 (53.0)	38.9, 67.1	500 (49.4)	40.5, 58.2
Spleen palpated	47 (9.7)	4.2, 15.3	26 (5.1)	0.4, 9.7	73 (7.3)	3.8, 10.9
Tasks related to common signs & symptoms of other causes of fever						
Cough	233 (47.2)	41.8, 52.6	167 (32.2)	25.0, 39.3	400 (39.5)	34.6, 44.4
Difficult breathing	37 (7.5)	5.6, 9.4	17 (3.3)	2.0, 4.6	54 (5.3)	4.0, 6.7
Chest pain	146 (29.6)	23.7, 35.4	78 (15.0)	13.3, 16.8	224 (22.1)	17.9, 26.3
Chest auscultated	109 (23.0)	15.8, 30.2	40 (7.8)	3.3, 12.3	149 (15.1)	10.5, 19.8
Running nose	51 (10.3)	6.9, 13.7	18 (3.5)	0.3, 6.7	69 (6.8)	4.3, 9.3
Throat pain	34 (6.9)	4.6, 9.1	23 (4.4)	2.2, 6.6	57 (5.6)	4.0, 7.2
Throat examined	42 (8.5)	4.8, 12.2	37 (7.1)	5.0, 9.3	79 (7.8)	5.8, 9.8
Ear problem	19 (3.9)	2.4, 5.3	9 (1.7)	0.4, 3.1	28 (2.8)	1.7, 3.8
Ear examined	19 (3.9)	2.4, 5.3	12 (2.3)	1.0, 3.6	31 (3.1)	2.1, 4.0
Breaths counted	4 (0.8)	0, 1.9	2 (0.4)	0, 0.9	6 (0.6)	0, 1.2
Vomiting	87 (17.6)	10.2, 25.0	129 (24.9)	16.8, 32.9	216 (21.3)	15.7, 27.0
Diarrhoea	60 (12.2)	6.2, 18.1	107 (20.6)	14.4, 26.9	167 (16.5)	11.8, 21.2
Lymph nodes palpated	4 (0.8)	0, 1.8	2 (0.4)	0, 0.9	6 (0.6)	0, 1.2
Urinary problem	30 (6.1)	3.4, 8.7	6 (1.2)	0, 2.3	36 (3.6)	2.0, 5.1

[a] Determined refers to performance of assessment tasks to detect signs and symptoms. Symptom was judged as determined if HW asked about its presence or the patient spontaneously reported the symptom. Sign was judged as determined if HW performed the task or the surveyor could obviously tell the patient had the information of interest

[b] Assessed means that either history of fever was assessed or temperature was measured

[c] Assessed means that either conjunctival or palmar pallor was checked; **CI** = confidence interval

5.3.5.2 Characteristics of the clinical assessment across age groups

Similar to the overall results, sub-optimal performance of clinical assessment tasks was demonstrated in both age groups (older children 5-14 years and adults above 14 years). Only 4 clinical tasks were more commonly performed in older children compared to adults and they were the following: determination of age (98.4% vs. 92.8%), assessment of history of fever (84.2% vs. 66.1%), vomiting (32.0% vs. 17.7%) and diarrhoea (23.7% vs. 4.3%). Assessment of joint pain (39.1 vs. 10.7) and chest pain (25.8% vs. 11.1%) was more commonly performed in adults than in children 5-14 years. For the remaining 24 assessment indicators measured, no statistically significant difference was observed between two age groups. Table 5.10 presents clinical assessment practices for patients with fever across two age groups.

Table 5.10: Clinical assessment practices for patients with fever across age groups

Health worker determined[a]	5-14 years (N=253)			≥15 years (N=760)		
	No	%	95% CI	No	%	95% CI
General tasks						
Age	246	98.4	96.8, 100	682	92.8	88.8, 96.8
Weight	14	5.6	1.6, 9.6	14	1.9	0.7, 3.1
Temperature	87	35.1	23.0, 47.2	176	23.5	15.6, 31.4
Initial or follow up visit	64	25.5	14.1, 36.9	195	26.4	16.4, 36.4
Previous use of drugs	145	57.3	48.1, 66.5	410	54.5	47.6, 61.5
Tasks related to common signs & symptoms of malaria						
History of fever	213	84.2	78.7, 89.6	502	66.1	58.8, 73.3
Fever assessed[b]	221	87.4	82.3, 92.4	537	70.7	63.6, 77.7
Duration of fever	129	51.2	36.5, 65.9	314	41.5	29.6, 53.4
Chills	57	22.5	15.6, 29.4	243	32.0	26.1, 37.8
Shivering	9	3.6	0.6, 6.5	36	4.7	3.0, 6.5
Headache	159	62.9	55.0, 70.7	454	59.7	54.5, 65.0
Joint pain	27	10.7	6.4, 14.9	297	39.1	34.7, 43.4
Conjunctival pallor	144	57.6	47.4, 67.8	346	46.2	36.9, 55.4
Palmar pallor	28	11.1	3.2, 19.0	45	6.0	1.6, 10.3
Pallor assessed[c]	147	58.1	47.9, 68.3	353	46.5	37.5, 55.4
Spleen palpated	22	8.7	3.8, 13.7	51	6.9	3.1, 10.6
Tasks related to common signs & symptoms of other causes of fever						
Cough	120	47.4	39.6, 55.3	280	36.8	31.9, 41.8
Difficult breathing	6	2.4	0.3, 4.5	48	6.3	4.7, 7.9
Chest pain	28	11.1	7.0, 15.2	196	25.8	21.0, 30.6
Chest auscultated	35	14.2	7.8, 20.5	114	15.4	10.6, 20.3
Running nose	23	9.1	4.4, 13.7	46	6.1	3.5, 8.6
Throat pain	8	3.2	0.2, 6.1	49	6.5	4.4, 8.5
Throat examined	13	5.1	1.8, 8.4	66	8.7	6.0, 11.4
Ear problem	9	3.6	1.3, 5.9	19	2.5	1.3, 3.7
Ear examined	11	4.4	1.9, 6.8	20	2.6	1.4, 3.9
Breaths counted	1	0.4	0, 1.2	5	0.7	0, 1.4
Vomiting	81	32.0	23.9, 40.2	135	17.7	12.4, 23.2
Diarrhoea	60	23.7	15.1, 32.3	33	4.3	10.1, 18.0
Lymph nodes palpated	2	0.8	0, 1.9	4	0.5	0, 1.1
Urinary problem	3	1.2	0, 2.5	33	4.3	2.4, 6.3

[a] Determined refers to performance of assessment tasks to detect signs and symptoms. Symptom was judged as determined if HW asked about its presence or the patient spontaneously reported the symptom. Sign was judged as determined if HW performed the task or the surveyor could obviously tell the patient had the information of interest.
[b] Assessed means that either history of fever was assessed or temperature was measured
[c] Assessed means that either conjunctival or palmar pallor was checked; **CI** = confidence interval

5.3.5.3 Detection of signs and symptoms with the current assessment practices

In this section the current health workers' performance of clinical assessment tasks was compared with the true presence of signs and symptoms established during the exit examination by study physicians. Such an analysis provides an estimate of the impact of the current assessment practices on the detection of each sign and symptom.

As presented in Section 5.3.5, the presence of fever was the most commonly assessed symptom (74.8%), however, 25.2% of fevers remained unobserved. Other malaria related signs and symptoms were less frequently detected: headache (69.7%), anaemia (57.4%), joint pain (43.8%), chills (36.7%), enlarged spleen (12.0%) and shivering (5.6%). The detection of these signs and symptoms was generally more frequent in Kisii than in Kwale district (Table 5.11). Of particular importance in the older children and adults age group, potential symptoms and signs commonly related to other causes of fever than malaria, have remained substantially undetected. The respiratory symptoms such as cough and chest pain were assessed in 63.9% and 55.5% of patients respectively when these symptoms were present. However, a throat problem was either examined or asked about in only 11.0% of patients with throat pain complaints or inflamed throat. Assessment of signs for which clinical examination is required generally showed lower detection rates compared to the symptoms based on history taking practices. For example, while gastrointestinal symptoms such as diarrhoea and vomiting were detected for the majority (69.2% and 55.6% respectively) of patients presenting with these symptoms, chest auscultation was performed for 28.0% of patients with an abnormal chest sound and lymph nodes were palpated in only 1.8% of patients with enlarged lymph nodes. There was no significant difference between districts in the assessment practices of symptoms and signs related to other causes of fever

than malaria. Table 5.11 presents the detection rate of the current assessment practices for each sign and symptom across two districts.

Table 5.11: Detection rates of various signs and symptoms with current assessment practices

Health worker determined[a]	KWALE			KISII			TOTAL		
	No[b]	%	95% CI	No[b]	%	95% CI	No[b]	%	95% CI
Signs and symptoms commonly related to malaria									
History of fever	307	63.2	56.5, 69.9	396	78.1	69.9, 86.3	703	70.8	64.5, 77.1
Temperature ≥37.5°C	36	39.6	23.2, 56.0	64	38.6	21.6, 55.5	100	38.9	27.1, 50.7
Fever[c]	339	68.6	60.8, 76.5	419	80.7	72.8, 88.6	758	74.8	68.6, 81.1
Headache	234	59.9	53.4, 66.3	320	79.2	73.2, 85.2	554	69.7	65.0, 74.3
Joint pain	105	36.1	28.1, 44.1	151	51.5	44.4, 58.6	256	43.8	38.3, 49.4
Chills	90	26.5	18.3, 34.7	165	46.6	39.8, 53.4	255	36.7	30.1, 43.4
Shivering	8	4.6	0.9, 8.4	7	7.5	2.7, 12.2	15	5.6	2.7, 8.5
Anaemia[d]	29	52.7	37.3, 68.1	6	100	NA	35	57.4	42.3, 72.5
Enlarged spleen	3	37.5	3.9, 71.1	3	7.1	0, 17.8	6	12.0	0, 24.3
Signs and symptoms commonly related to other causes of fever									
Cough	175	69.2	62.4, 75.9	113	57.1	48.1, 66.0	288	63.9	58.4, 69.3
Chest pain	117	54.9	49.7, 60.2	45	57.0	42.5, 71.4	162	55.5	50.4, 60.6
Running nose	37	20.3	12.9, 27.8	11	15.9	17.3, 30.2	48	19.1	12.7, 25.5
Vomiting	42	62.7	50.9, 74.4	72	52.2	41.2, 63.2	114	55.6	47.5, 63.7
Throat problem[e]	37	9.0	5.1, 12.8	19	20.0	12.7, 27.3	56	11.0	7.6, 14.4
Enlarged lymph nodes	2	1.9	0, 4.7	0	0	NA	2	1.8	0, 4.4
Diarrhoea	30	76.9	63.0, 90.9	33	63.5	52.1, 74.8	63	69.2	60.3, 78.2
Difficult breathing	13	25.5	12.7, 38.3	5	31.3	8.2, 54.3	18	26.9	16.2, 37.5
Abnormal chest sound	9	25.7	13.4, 38.0	5	33.3	0, 72.3	14	28.0	15.1, 40.9
Ear problem[f]	14	63.6	44.7, 82.6	6	46.2	13.1, 79.2	20	57.1	41.2, 73.0
Urinary problem	12	57.1	33.4, 80.9	1	7.1	0, 22.6	13	37.1	20.4, 53.8

[a] Determined refers to the performance of assessment tasks during observation of consultations to detect signs and symptoms established during the exit examination. Symptom was judged as determined if HW asked about its presence or the patient spontaneously reported the symptom. Sign was judged as determined if HW performed the task or the surveyor could obviously tell the patient had the information of interest

[b] Denominators for each sign and symptom are presented in Tables 5.4 and 5.5.

[c] Fever refers to assessment of history of fever or measurement of temperature

[d] Anaemia refers to assessment of conjunctival or palmar pallor

[e] Throat problem refers to assessment of throat either by asking for throat pain or performing throat inspection

[f] Ear problem refers to assessment of ear either by asking for ear problem or performing ear inspection

CI = confidence interval; **NA** = not applicable

5.3.6 Clinical predictors of malaria

To evaluate the ability of various signs and symptoms to detect malaria in febrile patients, data collected by study physicians during the exit examination were analysed. A "true" case of malaria was defined as a patient presenting with fever and detectible *P. falciparum* parasitaemia of any level (Sections 2.8.2.1. and 2.11.2). There were 43 malaria cases in Kwale district (22 in older children and 21 in adults) and 122 in Kisii district (56 in older children and 66 in adults). 14 patients with evidence of *non-P. falciparum* parasites were excluded from the analysis. Analysis was performed separately for older children and adults, however, due to the small sample of true malaria cases the district-specific analysis could not be performed and data from two districts were combined.

5.3.6.1 Clinical predictors - univariate analysis

In the univariate analysis the strength of association between each of 27 clinical predictors and malaria was estimated using logistic regression modelling and odds ratios with associated p-values were calculated for each investigated sign and symptom. The results of the univariate analysis revealed that 10 and 15 clinical predictors had p-values <0.20 in older children and adults respectively. Interestingly, symptoms and signs commonly related to malaria such as shivering and joint pain did not show any significant association with the measured outcome in any of two age groups. Similarly, no significant association was demonstrated for symptoms and signs commonly related to alternative causes of fever such as cough, diarrhoea and skin rash. Table 5.12 presents the odds ratios and p-values for each of 27 clinical predictors investigated in the two age groups.

Table 5.12: Clinical predictors of malaria across age groups: results of univariate analysis

	5-14 years				≥15 years			
	Malaria N = 78	Non-malaria N = 165	OR	p-value[a]	Malaria N = 87	Non-malaria N = 669	OR	p-value[a]
Symptoms								
Fever main complaint	57 (73.1)	103 (62.4)	1.63	**0.104**	42 (48.3)	298 (44.5)	1.16	0.511
Fever less than 7 days	63 (80.8)	134 (81.2)	0.97	0.934	68 (78.2)	382 (57.1)	2.69	**<0.001**
Chills	57 (73.1)	108 (65.5)	1.43	0.236	71 (81.6)	452 (67.6)	2.13	**0.009**
Shivering	27 (34.6)	45 (27.3)	1.41	0.243	23(26.4)	167 (25.0)	1.08	0.766
Headache	67 (85.9)	123 (74.6)	2.08	**0.049**	77 (88.5)	520 (77.7)	2.21	**0.023**
Joint pain	28 (35.9)	48 (29.1)	1.37	0.286	443 (66.2)	59 (67.8)	1.07	0.767
Backache	1 (1.3)	6 (3.6)	0.34	0.327	27 (31.0)	128 (19.1)	1.90	**0.011**
Vomiting	33 (42.3)	44 (26.7)	2.02	**0.015**	28 (32.2)	97 (14.5)	2.80	**<0.001**
Body weakness	30 (38.5)	61 (37.0)	1.07	0.823	38 (43.7)	343 (51.3)	0.74	**0.184**
General bodyache	2 (2.6)	0	NA	NA	11 (12.6)	58 (8.7)	1.52	0.229
Dizziness	8 (10.3)	11 (6.7)	1.60	0.334	17 (19.5)	80 (12.0)	1.79	**0.049**
Diarrhoea	17 (10.3)	57 (8.5)	1.14	0.771	6 (6.9)	57 (8.5)	0.80	0.607
Constipation	4 (5.1)	5 (3.0)	1.73	0.424	2 (2.3)	38 (5.7)	0.39	0.201
Abdominal pain	36 (46.2)	69 (41.8)	1.19	0.524	34 (39.1)	299 (44.7)	0.79	0.322
Nausea	18 (23.1)	30 (18.2)	1.35	0.372	21 (24.1)	189 (28.3)	0.81	0.421
Lack of appetite	7 (9.0)	7 (4.2)	2.23	**0.148**	1 (1.2)	28 (4.2)	0.27	**0.196**
Absence of cough	35 (44.9)	60 (36.4)	1.42	0.205	60 (69.0)	417 (62.3)	1.34	0.229
Absence of difficult breathing	77 (98.7)	155 (93.9)	4.97	**0.130**	85 (97.7)	615 (91.9)	3.73	**0.071**
Absence of running nose	54 (69.2)	99 (60.0)	1.50	**0.165**	77 (88.5)	526 (78.6)	2.09	**0.034**
Absence of chest pain	71 (91.0)	134 (81.2)	2.35	**0.054**	69 (79.3)	437 (65.3)	2.04	**0.010**
Signs								
Temperature ≥37.5°C	46 (59.0)	68 (41.2)	2.05	**0.010**	39 (44.8)	111 (16.7)	4.08	**<0.001**
Pallor	6 (7.7)	8 (4.9)	1.61	0.391	0	46 (7.0)	NA	NA
Palpable spleen	11 (14.1)	16 (9.7)	1.53	0.310	9 (10.3)	12 (1.8)	6.32	**<0.001**
Absence of throat problem[b]	52 (66.7)	87 (52.7)	1.79	**0.041**	58 (66.7)	302 (45.1)	2.43	**<0.001**
Normal chest sound	74 (94.9)	153 (92.7)	1.45	0.531	87 (100)	636 (95.1)	NA	NA
Absence of skin rash	63 (80.8)	138 (83.6)	0.82	0.581	83 (95.4)	628 (93.9)	1.35	0.572
Lymph nodes not enlarged	70 (89.7)	131 (79.4)	2.27	**0.051**	84 (96.6)	604 (90.3)	3.01	**0.067**

[a] In bold are p-values < 0.20
[b] The absence of throat infection on the inspection and/or history of throat pain
OR = odds ratio; **NA** = not applicable

5.3.6.2 Clinical predictors - multivariate analysis

To adjust for confounding, clinical predictors with a p-value < 0.20 from the univariate analysis (10 predictors in older children and 15 in adults) were entered into two age-specific multivariate logistic regression models. Using a backward elimination strategy

clinical predictors independently associated with malaria (odds ratios with p-value <0.05) were identified and sensitivities, specificities, and PPVs and NPVs were calculated.

The best fitting multivariate model to predict malaria in older children contained four clinical predictors: temperature ≥37.5°C, headache, vomiting and absence of chest pain. Older children possessing these symptoms were between 2.0 to 2.7 times more likely to have malaria. The final multivariate model in adults contained 6 clinical predictors with odds ratios more diverse than in older children. The predictors were: temperature ≥ 37.5°C (OR=3.77), fever duration of less than 7 days (OR=2.24), backache (OR=1.92), vomiting (OR=2.24), palpable spleen (OR=4.29) and absence of throat problem (OR=1.99). However, none of these independent symptoms and signs, neither in older children nor in adults, had sufficient sensitivity, specificity or predictive values to be useful as a diagnostic aid in a febrile patient. Table 5.13 presents the age-specific results of the multivariate analysis with attributed predictive values.

Table 5.13: Age-specific results of multivariate analysis with attributed predictive values

Older children (5 – 14 years)	**OR**	**p-value**	**Sens (%)**	**Spec (%)**	**PPV (%)**	**NPV (%)**
Temperature ≥37.5°C	1.97	0.020	59.0	58.8	40.4	75.2
Headache	2.40	0.026	85.9	25.5	35.3	79.3
Vomiting	2.14	0.013	42.3	73.3	42.9	72.9
Absence of chest pain	2.74	0.029	91.0	18.8	34.6	81.6
Adults (≥15 years)	**OR**	**p-value**	**Sens (%)**	**Spec (%)**	**PPV (%)**	**NPV (%)**
Fever less than 7 days	2.24	0.004	78.2	42.9	15.1	93.8
Backache	1.92	0.018	31.0	80.9	17.4	90.0
Vomiting	2.24	0.003	32.2	85.5	22.4	90.7
Absence of throat problem	1.99	0.007	66.7	54.9	16.1	92.7
Temperature ≥37.5°C	3.77	<0.001	44.8	83.4	26.0	92.1
Palpable spleen	4.29	0.004	10.3	98.2	42.9	89.4

OR = odds ratio; **Sens** = sensitivity; **Spec** = specificity; **PPV** = positive predictive value; **NPV** = negative predictive value

5.3.6.3 Clinical algorithms

A malaria score was calculated for each individual by a simple count of clinical predictors shown to be significantly associated with the measured outcome in the multivariate models. In older children the scores varied from 1 to 4 based on the following 4 signs and symptoms: temperature ≥37.5°C, headache, vomiting and absence of chest pain. In adults the scores varied from 1 to 6 based on the following 6 signs and symptoms: temperature ≥ 37.5°C, fever in duration of less than 7 days, backache, vomiting, palpable spleen and absence of throat problem. Predictive values of various scores were also compared with study physician diagnosis of malaria and current practice malaria diagnosis made by observed health workers.

In both age groups, none of the scores had sufficient sensitivity, specificity or predictive values to present an acceptable diagnostic aid in a febrile patient. However, in older children, in comparison to the current malaria diagnostic practice and a study physician diagnosis where major deficiencies were reflected in low specificities of 12.4% and 32.0% respectively, the score of 3 improved specificity to 61.2% but at the cost of poor sensitivity of 65.4%. Given the low prevalence of true malaria in the study sample size, even the most specific score of 4 could not increase positive predictive value more than 77.3%. Negative predictive values were generally high for all score values and diagnostic practices (range: 72.4-100%).

In adults, a score of 2 showed a sensitivity and specificity of 87.4% and 41.9% respectively, while a score of 3 improved significantly specificity (84.0%), however at

the cost of reduced sensitivity to 50.6%. The score of 3 showed improved specificity compared to the accuracy of physicians' diagnosis (33.9%) and current practices (16.7%). Predictive values of different scores from age-specific algorithms, accuracy of physician's and current practice malaria diagnosis are presented in Table 5.14.

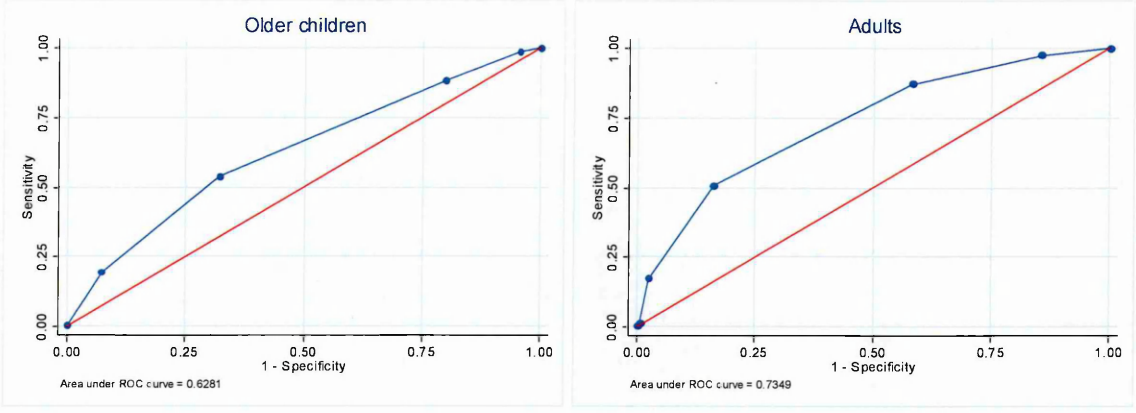
Table 5.14: Predictive values of different age-specific scores and accuracy of physician's and current practice malaria diagnosis

Older children (5 – 14 years)	**Sens (%)**	**Spec (%)**	**PPV (%)**	**NPV (%)**
Malaria score				
1	100	2.4	32.6	100
2	91.0	18.2	34.5	81.1
3	65.4	61.2	44.4	78.9
4	21.8	97.0	77.3	72.4
Physician's diagnosis[a]	87.7	32.0	38.1	84.5
Current practice[a]	95.9	12.4	34.3	86.4
Adults (≥15 years)	**Sens (%)**	**Spec (%)**	**PPV (%)**	**NPV (%)**
Malaria score				
1	97.7	14.5	12.9	98.0
2	87.4	41.9	16.3	96.2
3	50.6	84.0	29.1	92.9
4	17.2	97.6	48.4	90.1
5	1.2	99.4	20.0	88.6
6	0	100	0	88.5
Physician's diagnosis[a]	88.6	33.9	16.0	95.5
Current practice[a]	96.2	16.7	14.1	96.9

[a] Results adjusted for the exclusion of negative blood slides reported through routine practice
Sens = sensitivity; **Spec** = specificity; **PPV** = positive predictive value; **NPV** = negative predictive value

In both age groups the scores based on the selected signs and symptoms poorly performed, as demonstrated by small areas under the Receiver Operating Characteristic (ROC) curves shown in Figure 5.4. The areas under the ROC curves of the examined scores were only 0.63 (95% CI: 0.56-0.70) in older children and 0.73 (95% CI: 0.68-0.79) in adults.

Figure 5.4: Receiver operating characterteristic (ROC) curves for evaluated scores in older children and adults



5.4 Discussion

Three major findings of this study were: 1) The accuracy of the routine clinical malaria diagnosis was low, particularly characterised by a massive overdiagnosis of malaria; 2) the quality of the health worker's clinical assessment in considering alternative causes of fever was sub-optimal; and 3) the validity of the various clinical signs and symptoms to predict malaria was shown to be of very limited value as a diagnostic aid in febrile patients above 5 years of age.

5.4.1 Malaria prevalence and accuracy of the current clinical diagnosis of malaria

The presence of fever was the most common clinical presentation (80.5%) in older children and adults presenting to the outpatient departments of health facilities in both study districts. The large majority of febrile older children and adults (88.2%) were routinely diagnosed for malaria in both study districts. It appears that in both age groups, health workers', by presumptively diagnosing all fevers for malaria, use similar

diagnostic reasoning as previously demonstrated in young children below 5 years of age (Section 3.3.4.2).

The practice of equating nearly all fevers as malaria resulted in a high diagnostic sensitivity (95.2%), but at the cost of poor specificity (13.4%) demonstrated in both study districts and across both age groups. Although the prevalence of malaria parasitaemia was generally higher in Kisii (23.7%) than in Kwale district (11.3%), and in older children (30.8%) compared to adults (11.4%), the positive predictive values (PPV) of current malaria diagnostic practices remained low in both areas of different malaria transmission and all age groups (range: 8.2-41.6%). An overall PPV of 20.3% suggests that only 1 out of 5 routinely made malaria diagnoses in febrile patients actually have evidence of malaria infection. These observations are consistent with the results of the studies published from various health facilities across Africa where between 24 and 48% of adults treated for malaria had a positive malaria slide (Mkawagile & Kihamia, 1986; Jonkman *et al.*, 1995; Oster *et al.*, 2000).

As previously described in the literature (Trape & Rogier, 1996; Snow & Marsh, 1998) and also indicated by malaria age-specific prevalence curves in this study (Figure 5.1), clinical immunity develops with the age, the incidence of malaria disease declines as children get older, and the incidence is generally low in adults regardless of the level of malaria transmission. In this study low prevalence of malaria among febrile adult patients has been demonstrated in both districts; therefore, a massive overdiagnosis of true malaria in adults above 14 years of age cannot be regarded as an appropriate practice and

more conservative malaria diagnostic approaches focusing an alternative causes of fever are urgently required.

The interpretation of the results are more complex in children 5-14 years of age, where the incidence of malaria disease is generally higher than in adults but effective immunity is still being developed with the speed dependant on the intensity of malaria transmission. This study demonstrated that in areas of high malaria transmission such as Kwale district the prevalence of malaria in older children was significantly higher than in adults (20.0% vs 5.5%), however, it was low compared to 0-5 year old prevalence rates reported from the community surveys, and classifying the district as predominantly malaria hyper-endemic area (Section 2.3.3.4). Therefore, it is reasonable to conclude that in Kwale district clinical immunity, reflected in declined incidence of malaria in older children, has largely been acquired by the age of five. These conclusions suggest that in older children, like in adults, a similar malaria diagnostic approach should be applied and the current practice of presumptive diagnosis of all fevers for malaria should not be considered appropriate.

Given the highly seasonal pattern of malaria transmission in Kisii district, the timing of the survey during the malaria season and a high prevalence of malaria in older children (39.2%), the interpretation of the health workers' malaria diagnostic practices requires a more cautious approach among children aged 5-14 years. A higher prevalence of malaria disease in older children suggests a shift of the age-specific acquisition of functional immunity towards the older age groups above 5 years. However, it appears that even the

low intensity of transmission in Kisii district is sufficient to create some functional immunity by the age of 15 years, as reflected in significantly lower prevalence of malaria in adults (17.6%) compared to older children. This pattern has also been shown under a low transmission intensity setting in South Africa (Kleinschmidt & Sharp, 2001) and models of acquired immunity suggest that only a few parasite exposures are required to develop an immune response to the clinical consequences of infection (Snow *et al.*, 1994; Gupta *et al.*, 1999). Therefore, from a malaria risk point of view, in older children, as opposed to adults, the health workers presumptive diagnosis of all fevers as malaria may be an appropriate practice during the malaria seasons. However, in Kisii district, malaria diagnostic practices and their interpretations may be different outside the malaria season.

In the absence of diagnostics, a massive overdiagnosis of malaria in older children and adults could be explained by sub-optimal quality of clinical assessment of febrile patients and insufficient efforts to identify clinical presentations suggestive of alternative causes of fever. The quality of current clinical assessment of febrile patients is discussed in the following section.

5.4.2 Quality of clinical assessment in febrile patients

The various national and international malaria case management guidelines suggest a search for alternative causes of fever before establishing a malaria diagnosis and prescribing antimalarial treatment in older children and adults (MoH, 1998; WHO, 2000a). However, it has been suggested that the various predictors of alternative causes of fever will be dependent on their incidence, and acceptable criteria may differ between

different epidemiological settings (WHO, 2003a). As such, there are currently no recommendations on which signs and symptoms present sufficient criteria to exclude malaria and detect alternative causes of fever.

The review of the clinical presentations in this study revealed that malaria related symptoms such as headache, chills and joint pain are still the commonest clinical presentations in febrile older children and adults (symptom range: 57.7-78.5%). Yet, signs and symptoms commonly related to respiratory illnesses such as presence of cough, chest pain, throat problem and running nose are also frequently present (symptom range: 24.8-44.5%). Similarly, a substantial proportion of febrile patients presented with symptoms commonly related to gastrointestinal illnesses such as abdominal pain, vomiting and diarrhoea (symptom range: 9.0-43.2%). Common signs and symptoms of febrile patients with urinary problems, skin manifestations and other more obvious non-malaria related illness were rarely present. Some of the observed district specific differences in the frequencies of signs and symptoms, especially those related to the respiratory illnesses, are likely to be due to the lower prevalence of malaria in Kwale district, however, misclassification due to the use of different physicians between districts and possible discordant assessments cannot be excluded. Nevertheless, the frequent presence of signs and symptoms commonly related to diseases other than malaria such as respiratory or gastrointestinal illnesses may present an opportunity for health workers to perform a differential diagnosis and potentially identify alternative causes of fever before establishing a diagnosis of malaria.

However, the findings of our study revealed that none of the investigated signs and symptoms commonly related to the respiratory and gastrointestinal illnesses was considered in febrile patients in a proportion higher than 40%. Some of the respiratory symptoms such as cough, chest pain and running nose were more commonly assessed in Kwale than in Kisii district, however, these findings were more a reflection of a higher frequency of the respiratory symptoms in Kwale district and their spontaneous reporting by the patients than broader differential diagnosis performed by the health workers. Currently, it appears that the most of the health workers apply a vertical, presenting symptom based approach, with few exploratory assessment tasks being performed. As a result, a substantial proportion of the most common respiratory signs and symptoms (range: 36.1-89.0%), as well as gastrointestinal symptoms (range: 36.1-44.4%), remained unexplored and not considered when they were truly present. However, while such omissions in detecting various signs and symptoms may have an impact on under-diagnosing of other febrile illnesses, the sub-optimal quality of clinical assessment is of importance for the reduction of the current malaria overdiagnosis only if clinical predictors, sufficiently accurate to predict malaria, truly exist. In the following section the validity of the various clinical signs and symptoms to predict malaria in older children and adults are discussed.

5.4.3 Validity of the clinical signs and symptoms to predict malaria

This study detected 4 and 6 clinical predictors associated with malaria in older children and adults respectively. However, none of the investigated signs and symptoms had sufficient sensitivity and specificity to predict malaria in older children or in adults.

Increased axillary temperature had the best validity in older children (sensitivity and specificity of 59%) and the absence of throat problem had the best predictive power in adults (sensitivity 66.7%, specificity 54.9%). In both age groups, positive predictive values were lower than 50% for all investigated predictors, indicating that malaria diagnosis based on the best fitting individual predictors would continue to result in significant overdiagnosis of true malaria cases.

These observations are consistent with the few studies published on clinical predictors in older children and adults in Africa. In Kilifi district in Kenya, Mwangi *et al.* (2005) reported 9 and 3 signs and symptoms significantly associated with malaria parasitaemia in older children and adults respectively. However, predictors with the best individual accuracy such as cough not heard (sensitivity 72.0%, specificity 43.0%) in older children, and joint pains (sensitivity 25.8%, specificity 84.0%) in adults, still had an unsatisfactory predictive power to present a valid diagnostic aid. Similarly in Tanzania, Oster *et al.* (2000) reported that difficulties in breathing, sore throat, chest pain and cough, abnormal chest sound and enlarged lymph nodes were associated with a diagnosis other than malaria, however, the sensitivities of predictors presented were generally unsatisfactory (range: 17-55%) to be used as a diagnostic guide.

In this study the validity of different clinical scores created from signs and symptoms associated with malaria parasitaemia in the febrile patient did not significantly improve the accuracy of the malaria diagnosis compared to the individual predictors. In the study undertaken among adults living in an area of low malaria transmission in India, the best

performing score of 5 signs and symptoms had sensitivity of 54.6%, specificity of 57.5% and positive and negative predictive values of 14.7% and 90.5% respectively (Chandramohan *et al.*, 2001). Out of 10 signs and symptoms suggested in India, only 3 predictors (increased temperature, enlarged spleen and vomiting) remained part of the best fitting adult model in the population in the present study. Furthermore, in the study in Kilifi district in Kenya, 5 and 2 signs and symptoms were proposed as parts of the score models for older children and adults respectively (Mwangi *et al.*, 2005). Of all predictors proposed by the Kilifi study, only temperature $\geq$37.5°C in older children remained part of the best fitting models in the present two-district study. However, such differences are not surprising and were described previously, for example, the absence of cough was the only symptom from the proposed 9 predictors score in The Gambia (Olaleye *et al.*, 1998) that remained part of the model in the study in India (Chandramohan *et al.*, 2001). These findings highlight the point that clinical malaria predictors may vary between various malaria settings. Unfortunately, due to the small sample size of true malaria cases in this study, the data from the two districts had to be combined and the district specific differences in malaria predictors could not be investigated.

Weighted scores based on the strength of the association between individual predictors and the presence of malaria has been shown to improve the accuracy of the clinical predictors in The Gambia (Olaleye *et al.*, 1998; Bojang *et al.*, 2000). However, the use of weighted scoring systems complicates clinical malaria case definitions and is likely to further compromise accuracy of clinical predictors when implemented by the health

workers with limited training. This has also been suggested in The Gambia where further 7% of misclassification was generated when weighted scores were applied by the field workers (Bojang *et al.*, 2000).

5.4.4 Implications of study findings on national antimalarial drug policies

In Kenya, Snow *et al.* (2004) estimated that annual number of routine malaria diagnoses made at government facilities is 7.35 million, of which 4.82 million (65.6%) are made in older children and adult patients. Under current SP treatment policy, older children and adults consume 337,903 USD or 85.9% of all age antimalarial drug costs countrywide. If we assume, as suggested by the results of this study, that only 20.3% of malaria diagnoses made in older children and adults are truly malaria, it can be estimated that the annual unnecessary cost of current practices under SP treatment is 269,309 USD among older children and adult patient groups. However, the amount of unnecessary cost would substantially increase if the recently launched and more expensive artemether-lumefantrine (ART-LUM) treatment policy would be implemented under current diagnostic practices (MoH, 2004b); it can be estimated that only in older children and adults, the unnecessary cost for ART-LUM would increase to 8.6 million USD annually.

The results of this study suggest that significant improvements in malaria diagnostic accuracy cannot be achieved based on clinical signs and symptoms alone. For example, in comparison to the current practice, the best performing score of 2 would reduce the number of unnecessary malaria treatments in adults by only 2.2% while at the same time reasonably high sensitivity of 87.4% is preserved. In older children, a decrease in the

number of unnecessary treatments could not be achieved at all without increasing the rates of failure to treat up to unacceptable levels (37.4%). Therefore, the only potential cost-effective solution to improve malaria diagnostic accuracy under new and more expensive ART-LUM treatment policy is the use of malaria diagnostics. Traditionally, microscopy has been seen as a solution to this problem but it also has its limitations. The effects of microscopy on malaria case management in Kenya and the potential role of alternative malaria diagnostics are discussed in the following chapter.

CHAPTER 6:

Effects of microscopy on malaria case management

6.1 Introduction

6.1.1. Background

In most areas of sub-Saharan Africa the clinical diagnosis of malaria is often limited to a history of fever (Section 1.4.2). Since malaria is a disease that can rapidly progress to severe and potentially fatal complications if not treated early, low sensitivity of different clusters of signs and symptoms explored in the clinical predictors studies has been seen as a threat to the clinical management of the febrile child in malaria endemic areas (Marsh *et al.*, 1996; Chandramohan *et al.*, 2002). The conclusion of most studies was that parasitological confirmation is required to improve upon diagnostic accuracy.

While conventional first-line drugs, such as chloroquine and SP, are cheap and safe, significant over-treatment has to a certain degree been tolerated within international and national guidelines. However, with increased treatment failure rates to most of the first-line therapies in East Africa (EANMAT, 2003; Adjuik *et al.*, 2002) and the introduction of new, more expensive and more complex to use drugs with uncertain safety-margins (WHO, 2001a), the adequate use of laboratory diagnosis of malaria becomes far more important. Laboratory diagnosis of malaria would be expected to reduce the number of treated individuals but, in high malaria endemic areas, does not necessarily overcome the problem of asymptomatic, coincidental malaria parasitaemia in someone unwell for another reason.

Recognising the limitations of presumptive malaria diagnosis several countries in sub-Saharan Africa, including Kenya, have, to some extent, decentralised malaria microscopy

into peripheral health facilities. However, it remains unclear whether the provision of microscopy at the periphery of a health care system would have a sufficient impact on malaria case management and rational use of antimalarial drugs to justify the costs of establishing, maintaining and further expanding these services. The effectiveness of a strategy to provide microscopic malaria diagnosis is contingent on three factors: 1) the efficiency with which clinical staff use the service, 2) the accuracy of the blood smear examinations, and 3) the effect the results have on clinical management. If clinicians request malaria slides for incorrect indications, if blood slide results are inaccurately read, or if clinicians choose to ignore the results when prescribing the treatment, the value of having this service is compromised.

6.1.2. Malaria microscopy in Kenyan context and national recommendations

Since the early eighties, the Kenyan Ministry of Health has decentralised malaria microscopy to the level of all hospitals and most of the health centres. However, in practice a limited number of dispensaries and inter-level facilities such as sub-health centres may also have microscopes. Within the government health sector in Kenya, it has been estimated that approximately 50% of all outpatient malaria diagnoses are made at the level of health centres and hospitals (Snow *et al.*, 2000). Health facility databases developed prior to the surveys (Section 2.4) have shown that in four study districts (Kisii, Kwale, Bondo and Makueni) 2.9 facilities with microscopy were available per 100,000 people (district range: 2.1-3.2). A microscopic service was available in 42 (24.4%) of 172 government facilities (district range: 18.4-32.6%), in 28 (44.4%) of 63 mission facilities

(district range: 14.3-70.0%) and in 111 (38.0%) of 292 private facilities (district range: 18.2-44.9%).

National Policy Guidelines for Health Laboratory Services (MoH, 1995) specifies standards for laboratory structures and facilities, major equipment required, tests to be performed and laboratory staffing for each level of laboratory services. Within the district health system two levels of laboratory services are specified: peripheral, within health centres and dispensaries, and intermediate, within district hospitals. To some extent the guideline specifies standards related to malaria microscopy but only indicates that laboratories should have running tap water, power supply and binocular electric microscopes. The guideline further specifies that the staffing of laboratories at the peripheral level should include at least two laboratory technicians (trained for two years in basic laboratory disciplines) while the laboratories at the intermediate, district hospital level, should have twenty qualified laboratory workers of whom eight should be laboratory technologists (four years of laboratory training including a year of medical laboratory specialty). However, there are currently no officially recognised guidelines specifying standardised operating procedures for laboratory techniques, including microscopy.

The NMCP guideline promotes the use of microscopy wherever it is possible, however, it does not specify clinical indications for the use of microscopy and is ambiguous with regard to the interpretation of results. The guideline actually states: "*In certain cases a slide may be negative even when the patient has malaria. Conversely, malaria*

parasitaemia may not be the cause of the presenting illness" (MoH, 1998). The laboratory aspects of malaria case management are not addressed in the NMCP guideline. Kenyan country-specific IMCI guideline (MoH, 2000a), following recommendations from the international IMCI guideline (Gove, 1997), does not consider parasitological tests when diagnosing malaria in children <5 years and the guideline by definition does not address older children and adults.

This chapter presents observational data collected on current clinical and laboratory practices from the facilities with functional microscopy in four Kenyan districts. In this chapter the results of current effectiveness of malaria case management using microscopy are presented and the implications of the results on malaria diagnostic strategies in Kenya are discussed.

6.2 Methods

6.2.1 Study design and data collection

This survey was not primarily designed and statistically powered to measure the quality of routine microscopy and attributed case management practices across different age groups and levels of malaria endemicity; however, given the importance of the descriptive findings, the opportunistic data collected from health facilities with functional microscopy were considered valuable information to be presented in this chapter. Detailed presentation of the methods and materials used to conduct the health facility surveys is provided in Chapter 2.

Briefly, a series of cross-sectional, age-specific, cluster sample health facility surveys were conducted in the four districts (Kisii, Kwale, Bondo and Makueni) between July 2001 and April 2003. Surveys evaluating paediatric (< 5 years of age) outpatient malaria case management practices were conducted in each of the four districts, while surveys studying older children and adult (≥ 5 years of age) practices were undertaken in Kisii and Kwale districts.

Of relevance for this chapter, clinical practices in relation to microscopy (diagnostic procedures requested, results reported and medications prescribed) were recorded from patient-held records either during the exit caretaker interview during paediatric surveys or during the exit examination in surveys of older children and adults. A child < 5 years was considered to have fever if the caretaker told the interviewer that the child had fever as part of the presenting illness. A patient ≥ 5 years was considered to have fever if this symptom was reported to have occurred over the last 48 hours or axillary temperature measured during the exit examination was ≥ 37.5°C.

During the older children and adult survey, if a blood slide was requested during the initial health worker consultation, the study finger prick sample was performed simultaneously with the same drop of blood in the clinical laboratory and thick and thin blood films were prepared and stained with 10% Giemsa by the laboratory technician. After the completion of the survey two expert microscopists read all slides independently and the third reading was performed for the discordant results. For each slide 100 high power magnification fields were examined before the slide was regarded as negative. The

number of parasites per 200 white blood cells (WBC) was counted. Parasite density/μl of blood was calculated assuming an average leukocyte count of 8,000 WBC/μl of blood.

Characteristics of the surveyed laboratories were collected either during the health facility assessment through interviews with the laboratory in-charges or the data were obtained from the health facility database developed for the study districts prior to the surveys. The characteristics of the clinicians who managed the patients were collected during the health worker interview.

6.2.3 Statistical analysis

The data for each age-specific survey were aggregated and presented combined for all districts together. However, because of the structure of the different surveys and possible variations in the practices between age groups and areas of malaria endemicity, the analysis, where possible and appropriate, was carried out separately across four age groups (< 1 year, 1-4 years, 5-14 years and ≥15 years) and two areas of endemicity (*high* - Kwale and Bondo districts, and *low* – Kisii and Makueni districts). The precision of proportions (95% confidence interval) was estimated accounting for the cluster sampling design.

To analyse the accuracy of the routine reading of malaria slides during older children and adult survey, the gold standard was defined as parasitaemia determined by two expert microscopists. The sensitivity, specificity, and positive and negative predictive values were calculated according to the following formula: *Sensitivity* = routine malaria slide

reported as positive / positive slide reported by expert microscopists; *Specificity* = routine malaria slide reported as negative / negative slide reported by expert microscopists; *Positive predictive value* (PPV) = positive slide reported by expert microscopists / routine malaria slide reported as positive; *Negative predictive value* (NPV) = negative slide reported by expert microscopists / routine malaria slide reported as negative.

6.3 Results

6.3.1 Description of the survey samples

The paediatric survey was undertaken at the outpatient departments of 34 government health facilities with functional microscopy where 73 health workers were observed performing 1015 sick child consultations. Of 1015 consultations, the exit interview could not be performed with 129 (12.7%) caretakers and these children were excluded from the analysis. The older children and adult survey was undertaken at the outpatient departments of 17 government health facilities with functional microscopy where 31 health workers were observed performing 456 consultations. Of 456 consultations, 26 patients (5.7%) were excluded from the analysis because they did not have the exit examination performed. The distribution of the health facilities with functional microscopy, health workers and analysed health worker-patient consultations across four districts and two age-specific surveys are presented in Table 6.1.

Table 6.1: Distribution of the health facilities with functional microscopy, health workers and analysed health worker-patient consultations across four districts: results from two age-specific surveys

District	Kisii		Kwale		Bondo		Makueni		Total	
Age-specific survey	< 5	≥5	< 5	≥5	< 5	≥5	< 5	≥5	< 5	≥5
Health facilities	10	7	10	10	4	NA	10	NA	34	17
Health workers	21	14	22	17	10	NA	20	NA	73	31
Consultations	288	210	230	218	156	NA	212	NA	886	428

NA = not available since older children and adult survey was not performed in Bondo and Makueni districts

6.3.2 Characteristics of the laboratories with functional microscopy

The assessment of 34 health facilities revealed that the majority of the surveyed laboratories were within health centres (55.9%), followed by hospitals (29.6%) and dispensaries (14.7%). Running water and electricity was available in 50.0% and 55.9% of laboratories, respectively. Most laboratories were equipped with only light microscopes (52.9%) while electric microscopes were available in 35.3% of facilities. Both types of microscopes were available only at the four district hospitals. At least one laboratory technologist was posted in 41.2% of the surveyed facilities, while 88.2% of laboratories were staffed with laboratory technicians. In-charges of laboratories reported that both thick and thin films were routinely performed in only 23.5% of facilities. In the majority of facilities (76.5%) only a thick film was used for the preparation of malaria slides. Field stain was most commonly used as the routine staining method for malaria microscopy (70.6%), while Giemsa staining was routinely done in 10 laboratories (29.4%). Routine performance of species differentiation was reported from approximately half of the laboratories (52.9%). However, this finding was not confirmed by reviewing the patients' laboratory reports (Section 6.3.5). The majority of the laboratory in-charges (76.5%) reported that parasite densities were routinely counted for positive slides using semi-quantitative methods (plus or a descriptive scoring system). No laboratory sent malaria

slides for quality control. Characteristics of the surveyed laboratories are presented in Table 6.2.

Table 6.2: Characteristics of the surveyed laboratories with functional microscopy

Laboratory characteristics	*N=34[a] (%)*
Laboratory within:	
District Hospital	4 (11.8)
Sub-district hospital	6 (17.7)
Health centre	19 (55.9)
Dispensary	5 (14.7)
Electricity available	19 (55.9)
Running water available	17 (50.0)
Laboratory technologist available	14 (41.2)
Laboratory technician available	30 (88.2)
Type of microscope available	
Light	18 (52.9)
Electric	12 (35.3)
Light and electric	4 (11.8)
Type of malaria films routinely prepared	
Thick film only	26 (76.5)
Thick and thin film	8 (23.5)
Routine staining method performed	
Field stain	24 (70.6)
Giemsa	10 (29.4)
Species differentiation routinely performed	18 (52.9)
Parasite densities routinely counted	26 (76.5)
Malaria slides sent for quality control	0

[a] Information collected only during the children survey from 34 health facilities including 15 out of 17 facilities repeatedly surveyed during the older children and adult study

6.3.3 Characteristics of health workers who used microscopic services

During the paediatric survey, none of the 73 health workers refused to participate in the study. However, of 73 health workers, 6 (8.2%), who performed a total of 56 consultations, urgently left the health facility before an interview could be performed. During the older children and adult survey, the interview was completed with all of 31 participating health workers. Clinical officers performed the majority of consultations (58.4% in the paediatric survey and 59.2% in the older children and adult survey). In both

surveys, approximately half of the health workers received malaria in-service training and had the NMCP guideline. No health worker received IMCI training. The characteristics of health workers who used microscopic services are presented in Table 6.3.

Table 6.3: Characteristics of observed health workers who used microscopic services: results from two age-specific surveys

Health workers characteristics	< 5 years	≥ 5 years
	N=67 (%)	*N=31 (%)*
Male sex	37 (55.2)	19 (61.3)
Pre-service training		
Clinical officer	30 (44.8)	16 (51.6)
Nurse	35 (52.2)	14 (45.2)
Nursing aide	2 (3.0)	1 (3.2)
HW received in-service malaria training	27 (40.3)	15 (48.4)
HW received IMCI training	0	0
HW possessed NMCP guideline	38 (56.7)	18 (58.1)

HW = health worker

6.3.4 Utilisation of malaria blood slides

In both age groups, an equal proportion (80%) of patients presented with fever (95% $CI_{<5}$: 77.1-84.0; 95% $CI_{\geq 5}$: 74.0-86.3). Of 886 children and 428 older children and adults included in this analysis, only 2.4% of children and 6.1% of patients ≥ 5 years of age had a malaria slide requested but not subsequently performed. However, this figure may be underestimated since among all observed patients who were referred to laboratory 13.4% of children and 9.0% of older children and adults were lost to follow up since they did not have an exit interview or exit examination completed. These patients were excluded from the analysis and the reason for loss to follow up could not be established, however, it could be assumed that the majority of them had not returned to the consultation room and for the exit interview because the requested malaria slide may not have been

performed. Therefore, the proportion of patients, adjusted for the loss in follow up, with a malaria slide requested but not performed, could have reached 15% in both age groups.

Among all outpatients included in the analysis, a malaria blood slide was more frequently performed in older children and adults (74.3%, 95% CI: 61.9-86.7) than in children < 5 years of age (48.8%, 95% CI: 39.0-58.5). A very similar pattern was revealed in patients with fever (Table 6.4). Furthermore, in both patient populations (all outpatients and febrile patients), a malaria slide was less frequently performed in infants in comparison to the other age groups; however, the difference was not statistically significant in comparison to the 1-4 year age group (see CIs in Table 6.4). Statistically significant differences were observed between the requests for a malaria slide for non-febrile patients and different age groups. Among 172 non-febrile patients <5 years of age, a malaria blood slide was performed for 20.9% (95% CI: 13.8-28.9) children. In older children and adults, among 85 non-febrile patients a blood slide was performed for 52.9% (95% CI: 29.2-76.7) patients. Table 6.4 presents presents the pattern of malaria blood slide utilisation across age groups and presence of fever.

Table 6.4: Utilisation of malaria blood slides across age groups and presence of fever

	< 1 year		1-4 years		5-14 years		≥ 15 years	
	No (%)	**95% CI**	**No (%)**	**95% CI**	**No (%)**	**95% CI**	**No (%)**	**95% CI**
All patients	N=333		N=553		N=92		N=336	
	132 (39.6)	28.2, 51.1	300 (54.3)	44.7, 63.8	73 (79.3)	67.0, 91.7	245 (72.9)	59.9, 85.9
Febrile patients	N=257		N=457		N=78		N=265	
	116 (45.1)	32.9, 57.4	280 (61.3)	51.2, 71.4	66 (84.6)	75.0, 94.2	207 (78.1)	68.2, 88.1

CI = confidence interval

6.3.5 Laboratory reports of routine malaria microscopy

Among all patients who had a blood slide performed (432 children < 5 years and 318 patients ≥ 5 years), 59.5% (95% CI: 50.6-68.4) children and 43.4% (95% CI: 31.2-55.6)

older children and adults had a positive blood slide reported through routine microscopic practices The routine reports of positive malaria slides demonstrate the usual malaria prevalence trends in relation to the age groups and different levels of endemicity, although none of the comparisons were statistically significant (Table 6.5). In high endemic areas, the trend suggests high levels of positivity in infants (59.7%) followed by a slight increase in children 1-4 years (62.8%) and subsequent decrease in older children (40.0%) and in particular in adults (21.6%). In low endemic areas, the infants had a lower proportion of positive slides reported (41.8%) compared to high endemic areas. Furthermore, the positivity rate in children 1-4 years of age was identical to the areas of high endemicity (62.6%) and remained rather stable in older age groups such children 5-14 years (64.6%) and adults (52.5%).

Table 6.5: Malaria blood slide positivity rates across age groups and the levels of malaria endemicity: results of routine microscopic practices

Endemicity	< 1 year		1-4 years		5-14 years		≥ 15 years	
	No (%)	95% CI	No (%)	95% CI	No (%)	95% CI	No (%)	95% CI
High[a]	46 (59.7)	47.3, 72.1	76 (62.8)	50.2, 75.4	10 (40.0)	19.8, 60.2	22 (21.6)	7.8, 35.4
Low[b]	23 (41.8)	25.7, 57.8	112 (62.6)	46.6, 78.6	31 (64.6)	55.4, 73.8	75 (52.5)	32.8, 72.1

[a] Results from Kwale and Bondo districts in children < 5 years and Kwale district in patients ≥ 5 years
[b] Results from Kisii and Makueni districts in children < 5 years and Kisii district in patients ≥ 5 years

The majority of patients (70.0% children and 60.1% older children and adults) with a routinely reported positive malaria slide had parasite densities quantified and reported either by using a plus scoring (one to four pluses) or descriptive (scanty, moderate, numerous and heavy) system. However, a significant proportion of patients had positive results reported without quantifying any parasite densities (30.0% and 39.9% in each age-specific survey). Among all positive malaria slides, the most common laboratory report

included a one-plus score or scanty parasitaemia (46.7% in children < 5 years and 51.4% in patients ≥ 5 years). Only 23.3% children <5 years of age and 8.7% older children and adults had any other parasite density reported than one plus or scanty. Of interest, among 71 patients ≥ 5 years of age with one plus or scanty parasitaemia routinely reported, only 6 (8.5%) were confirmed as positive on expert microscopy. Furthermore, contrary to the information obtained from the interviews with laboratory in-charges (Section 6.3.2), none of the positive reports contained specification of *Plasmodium* species. Laboratory reporting of parasite densities for positive malaria slide results are presented in Table 6.6.

Table 6.6: Laboratory reports of parasite densities for positive malaria slide results: results of routine practices from two age-specific surveys

Parasite densities reported	< 5 years		≥ 5 years	
	N=257 (%)	95% CI	N=138 (%)	95% CI
+ /scanty	120 (46.7)	33.3, 60.1	71 (51.4)	26.3, 76.4
++/moderate	35 (13.6)	9.9, 17.4	9 (6.5)	1.1, 11.9
+++/numerous	4 (1.6)	0, 3.3	0	NA
++++/heavy	21 (8.1)	5.9, 11.1	3 (2.2)	0, 5.0
Not quantified	77 (30.0)	21.5, 38.8	55 (39.9)	13.2, 66.6

CI = confidence interval; **NA** = not applicable

6.3.6 Interpretation of malaria blood slide results

Nearly all patients with reported positive malaria slide received antimalarial treatment (four age-group range: 95.1-98.9%). Similarly, health workers prescribed an antimalarial treatment for the majority of patients with a reported negative malaria slide: in children <5 years of age, 119 of 175 patients (68.0%, 95% CI: 57.8-78.2) with a negative slide result were given an antimalarial; in older children and adults, 139 of 180 patients (77.2%, 95% CI: 66.2-88.3) received antimalarial treatment when a malaria slide was reported negative. In the analysis across four age groups, the pattern and magnitude of

this practice remained the same and no significant differences between the age groups were revealed. Approximately half of the patients with positive slide result received antibiotic treatment in children <5 years of age (130 of 257; 50.6%, 95% CI: 40.7-60.5) as well as in older children and adults (69 of 138; 50.0%, 95% CI: 40.4-59.6). The majority of patients with reported negative slide result had received antibiotic treatment (four age-group range: 56.1-81.0%). The antipyretic treatments were also prescribed for large majority of the patients regardless of the blood slide results (four age-group range: 66.7-95.1%). The relationship between antimalarial, antibiotic and antipyretic prescriptions and blood slide results across age groups is presented in Table 6.7.

Table 6.7: Prescriptions of antimalarial, antibiotic and antipyretic drugs according to the reported malaria slide result and age groups

	< 1 year			1-4 years			5-14 years			≥ 15 years		
	No	%	95% CI	No	%	95% CI	No	%	95% CI	No	%	95% CI
Positive slide	N=69			N=188			N=41			N=97		
AM prescribed	67	97.1	92.8, 100	186	98.9	97.3, 100	39	95.1	87.6, 100	93	95.9	92.4, 99.3
AB prescribed	36	52.2	35.6, 68.8	94	50.0	39.3, 60.7	27	65.9	47.3, 84.4	42	43.3	28.7, 57.9
AP prescribed	58	84.1	73.9, 94.2	160	85.1	78.9, 91.4	39	95.1	87.6, 100	92	94.9	90.2, 99.5
Negative slide	N=63			N=112			N=32			N=148		
AM prescribed	42	66.6	54.4, 78.9	77	68.8	56.9, 80.6	24	75.0	57.6, 92.4	115	77.7	66.7, 88.7
AB prescribed	51	81.0	71.2, 90.7	77	68.8	59.6, 77.9	19	59.4	46.8, 72.0	83	56.1	45.0, 67.1
AP prescribed	42	66.7	55.4, 78.0	80	71.4	61.3, 81.6	27	84.4	67.6, 100	134	90.5	83.1, 98.0

CI = confidence interval; **AM** = antimalarial; **AB** = antibiotic; **AP** = antipyretic

The analysis of antimalarial, antibiotic and antipyretic prescriptions for a negative malaria slide across age groups did not reveal significant differences between areas of different malaria endemicity (Table 6.8). However, it was observed that infants received more commonly antibiotic treatment than patients ≥ 15 years, the difference being statistically significant only in area of high endemicity. The relationship between

negative blood slide result and antimalarial, antibiotic and antipyretic prescriptions across two levels of malaria endemicities and age groups is presented in Table 6.8.

Table 6.8: Prescriptions of antimalarial, antibiotic and antipyretic drugs for negative malaria slides across age groups and the levels of malaria endemicity

	< 1 year			1-4 years			5-14 years			≥ 15 years		
	No	%	95% CI	No	%	95% CI	No	%	95% CI	No	%	95% CI
High endemicity	N=31			N=45			N=15			N=80		
AM prescribed	20	64.5	44.9, 84.2	28	62.2	48.9, 75.5	13	86.7	53.3, 100	60	75.0	55.7, 94.2
AB prescribed	25	80.7	67.4, 93.9	27	60.0	43.9, 76.1	8	53.3	36.9, 69.7	40	50.0	33.0, 67.0
AP prescribed	24	77.4	64.7, 90.1	36	80.0	64.9, 95.1	12	80.0	44.8, 100	71	88.8	75.8, 100
Low endemicity	N=32			N=67			N=17			N=68		
AM prescribed	22	68.8	51.5, 86.0	49	73.1	55.2, 91.1	11	64.7	43.3, 86.1	55	80.9	71.0, 90.8
AB prescribed	26	81.3	64.8, 97.7	50	74.6	64.4, 84.9	11	64.7	43.3, 86.1	43	63.2	51.7, 74.8
AP prescribed	18	56.3	36.8, 75.7	44	65.7	53.6, 77.7	15	88.2	67.4, 100	63	92.7	85.8, 99.5

CI = confidence interval; **AM** = antimalarial; **AB** = antibiotic; **AP** = antipyretic

6.3.7 Accuracy of the routine malaria microscopy

During older children and adult survey malaria slide results reported by routine microscopic services were compared with the gold standard result, and sensitivity, specificity and positive and negative predictive values were calculated. A total of 318 routine malaria slides were evaluated. The slide positivity rate of expert microscopy was 14.5% (95% CI: 9.1-19.8), without significant difference between the districts of high and low malaria transmission: 10.2% (95% CI: 5.4-15.1) of blood slides in high endemic Kwale district and 17.3% (95% CI: 8.9-25.7) in low endemic Kisii district were malaria positive on the expert microscopy. Using data pooled across both districts the sensitivity and the specificity of the routine microscopy were 67.4% and 60.7% respectively. The positive predictive value was very low (22.5%), while the negative predictive value was significantly higher (92.7%). The results on accuracy of routine blood slide microscopy are presented in Table 6.9.

Table 6.9: Accuracy of the routine malaria microscopy

	No/N	%	95% CI
Slide positivity rate (expert microscopy)	46/318	14.5	9.1, 19.8
Sensitivity	31/46	67.4	56.1, 78.6
Specificity	165/272	60.7	47.1, 74.3
Positive predictive value	31/138	22.5	12.6, 32.3
Negative predictive value	165/180	91.7	87.6, 95.7

CI =confidence interval

Regardless of the levels of endemicity positive slides reported by routine practices were rarely confirmed as such by the expert microscopists (PPV_{high}=21.9% and PPV_{low}=22.6%). Conversely, in both areas of malaria endemicity routine slides reported as negative were in most cases truly confirmed as negative (NPV_{high}=93.7% and NPV_{low}=89.4%). Furthermore, the specificity in low endemic areas was significantly lower compared to high endemic areas (SP_{low}=48.1% and SP_{high}=78.1%). Conversely, sensitivity of routine microscopy was higher in areas of low endemicity (SE_{low}=72.7% and SE_{high}=53.9%), however the difference was not statistically significant. The results on the accuracy of blood slide microscopy in relation to the level of malaria endemicity are presented in Table 6.10.

Table 6.10: Accuracy of the routine malaria microscopy: results from two areas of malaria endemicity

	Low endemicity[a]			High endemicity[b]		
	No/N	%	95% CI	No/N	%	95% CI
Slide positivity rate (expert microscopy)	33/191	17.3	8.9, 25.7	13/127	10.2	5.4, 15.1
Sensitivity	24/33	72.7	57.3, 88.2	7/13	53.9	24.3, 83.4
Specificity	76/158	48.1	29.0, 67.2	89/114	78.1	70.4, 85.7
Positive predictive value	24/106	22.6	7.6, 37.7	7/32	21.9	10.4, 33.4
Negative predictive value	76/85	89.4	81.0, 97.9	89/95	93.7	90.5, 96.5

[a] Low endemic area - Kisii district
[b] High endemic area - Kwale district

6.4 Discussion

It is expected that the introduction of microscopy into health facilities in Kenya would assist health workers to differentiate malaria from other fever-causing conditions and prompt diagnosis of other diseases, reduce unnecessary wastage of antimalarial drugs and potentially reduce the likelihood of emerging antimalarial drug resistance. It should be acknowledged that in the absence of any standard operating procedures for laboratories, recommendations on the clinical indications for the use of malaria microscopy and ambiguous instructions in the clinical guidelines on the interpretation of malaria slide results, a rigorous study of the quality of malaria case management at facilities with microscopy is difficult. However, the magnitude of the descriptive observations made in this study highlight a series of irrational practices which compromise effectiveness of malaria case management and indicates a need for careful review of malaria diagnostic strategies using microscopic services countrywide.

Three major findings in this study were: 1) malaria microscopy was a commonly requested and performed laboratory investigation, however, clinical indications for its use were frequently inappropriate; 2) clinical interpretation of malaria blood slide results was frequently irrational, in particular for the patients with a negative slide result; and 3) the quality of malaria microscopy and the accuracy of routine malaria slide readings was sub-optimal. The possible explanations for such findings across different patient populations are discussed in the following three sections while the implications of the findings on malaria diagnostic strategies in Kenya are discussed in the last section of the chapter.

6.4.1 Clinical utilisation of microscopy

In all age groups, the importance of microscopic diagnosis is well recognised, a malaria slide was commonly requested, and for the large majority of laboratory requests an investigation was performed. Interestingly, older children and adults were more frequently referred for microscopy compared to children 1-4 years of age and infants (74.3% vs 54.3% vs 39.6 respectively). Utilisation of malaria blood slides in our survey was significantly higher than reported in Zambia, where 30% of children below 5 years of age and 25% of all outpatients were sent for microscopy (Barat *et al.*, 1999). Several reasons may explain the higher use of microscopy in adults compared to children in the present study. First, health workers may still consider microscopy less important among febrile children since it interferes with the traditional concept of equating all fevers with malaria, therefore, they do not see the same justification for microscopy compared to adults where a diagnosis of exclusion has been traditionally promoted. In children this practice seems pragmatic and reflects IMCI recommendations, however, the value of requesting a slide at all may be questioned in this patient group. Second, since malaria microscopy frequently presents an additional cost, ranging from 10-50 KES (Tetteh & Mwangi, 2004) an economically more vulnerable group, such as mothers of children, may be less able to pay for this service compared to sick adults. Third, health workers may be more susceptible to articulated pressures by adult patients than mothers with sick children to perform a parasitological investigation, as this may be considered as an "expected" part of the consultation.

An interesting finding of this study was that a substantial proportion of children (20.9%) without any signs or symptoms of fever were referred for microscopy. Moreover, in the older children and adult patient groups, more than half (52.9%) of non-febrile patients were referred for microscopy. These findings are in accordance with the results reported from Bungoma district in Kenya, where 40% of all non-febrile patients were referred for microscopy (Barat & Kramer, 1999), however, they are significantly higher than 9% reported in Zambia (Barat *et al.*, 1999). Possible explanations for such irrational practices may include: 1) a deficiency in health workers knowledge on the role of fever in malaria; 2) lack of instructions in the national malaria guidelines on the clinical indications for the use of malaria microscopy; or 3) patients expectations for microscopy regardless of the clinical presentation.

6.4.2 Clinical interpretation of malaria slide results

The alarming finding in this study is that the majority of patients across all age groups with reported negative blood slide result subsequently received an antimalarial treatment (68.8% in children and 77.2% in older children and adults). Furthermore, such practice was equally present in low and high malaria endemic areas. The introduction of microscopes into a hospital in Malawi decreased significantly the number of unnecessary antimalarial prescriptions in adults and produced annual savings of 3% of annual drugs budget for the hospital (Jonkman *et al.*, 1995). However, during the study in Malawi all clinicians strictly adhered to the recently introduced guidelines, prescribing antimalarial drugs only to parasitaemic patients.

In the studies performed under routine practice conditions in Kenya, Zambia and Benin the experiences are different. In the present study, the magnitude of antimalarial treatment practice ignoring the negative malaria slide was similar (67.3%) to the practice in Benin (Holtz & Kachur, 2000), and greater compared to the 30% reported from Zambia (Barat *et al.*, 1999) and 39% reported from Bungoma district in Kenya (Barat & Kramer, 1999). In a study targeting broader spectrum of conditions in six health centres across Kenya, the laboratory use changed clinician's diagnosis in 45% of patients tested and only 21% of all outpatients with new condition (Carter & Lema, 1999). Findings from the inpatient setting in Tanzania revealed that only 13.3% of admitted patients with a clinical diagnosis of cerebral malaria had a positive blood slide (Makani *et al.*, 2003). This practice, present at such a large scale, showed that probably the only major effect of the microscopic service is increasing cost to poor patients with little rational effect on use of antimalarial drugs.

For instance, in the four study districts, the average annual number of reported malaria diagnoses from 42 health facilities with microscopic services between 1996 and 2001 was 232,294 (HMIS, 2001; Snow *et al.*, 2004). Using the study age-specific data on the utilisation of microscopy, routine blood slide positivity, and the antimalarial prescription practices, the annual average costs of different treatment regimens were calculated and the differences in the treatment costs between the current practice and the practice adjusted to respect negative malaria slides were compared. In Table 6.11 the calculation process of the average four-district annual costs of SP and ART-LUM treatments according to different diagnostic practices and across age groups is presented.

Assuming conservatively that all patients had received the cheapest antimalarial drug (SP) it was calculated that the incurred cost of SP treatment under the current diagnostic practice is 3,165 USD per average district on an average year. However, only a single change of practice at facilities with microscopic services, such as respect of negative parasitological results, would reduce cost of SP treatment by 41.3% and generate annual saving of 1,308 USD per average district on an average year. Of the 1,308 USD annual saving per district, 94.1% or 1,231 USD would be saved by respecting negative slides in older children and adult age groups (patients ≥ 5 years of age).

With the change of treatment policy from SP to 30-fold more expensive ART-LUM (2.4 USD adult treatment course), respect of negative parasitological results at facilities with microscopy would produce an average district annual saving of 43,475 USD on an average year, of which 90.0% or 39,123 USD per district would be created by changing the practice only in older children and adult age groups. These findings suggest that from the cost perspective microscopy in older children and adults has a large potential to reduce the number of unnecessary antimalarial treatments and create significant savings in antimalarial drug budgets. It might, however, be argued that the reduction in use of antimalarials would increase prescription of symptomatic and other antimicrobial treatments and compensate for the cost-savings on antimalarial drugs. Given that the majority of older children and adults with positive and negative slide results were currently prescribed inexpensive antipyretics (94% for positive and 89% for negative results) and antibiotics (50% for positive and 57% for negative results) anyway, it is not obvious that replacement costs would significantly undermine potential savings.

Table 6.11: Average annual costs of SP and ART-LUM treatments according to different diagnostic practices and across age groups – results from 42 facilities with microscopy in four study districts

	<1 year	1-4 yrs	5-14 yrs	≥ 15 yrs	All ages
Morbidity					
No of malaria diagnoses[a]	24,452	50,251	48,465	109,126	232,294
No of all outpatients[b]	37,502	67,451	63,687	152,198	320,838
Utilisation of microscopy[c]					
No of patients with performed BS	14,851	36,626	50,503	110,952	212,932
No of patients without BS performed	22,651	30,825	13,184	41,246	107,906
Positivity rate[d]					
No of patients with positive BS	7,767	22,965	28,382	43,937	103,051
No of patients with negative BS	7,084	13,662	22,121	67,015	109,882
Antimalarial (AM) prescription practices					
a) No of AM treatments when BS positive[e]	7,542	22,712	26,991	42,135	99,380
b) No of AM treatments when BS negative[f]	4,718	9,399	16,591	52,071	82,779
c) No of AM treatments when BS not done[g]	12,164	18,156	4,852	14,972	50,144
Different diagnostic practices					
No of AM treatments under current practice (a+b+c)	24,423	50,267	48,434	109,178	232,302
No of AM treatments respecting BS negative result (a+c)	19,706	40,868	31,843	57,107	149,524
Cost of different practices (USD)					
a) Cost of SP[h] - current practice	318	1,307	2,519	8,516	12,660
b) Cost of SP - BS negative result respected	256	1,063	1,656	4,454	7,429
c) Cost of ART-LUM[i] - current practice	21,981	70,374	92,025	262,027	446,407
d) Cost of ART-LUM - BS negative result respected	17,735	57,215	60,502	137,057	272,509
Average annual savings					
Savings on SP (USD) (a-b)	61	244	863	4,062	5,230
Age-specific percent of total saving on SP	1.2	4.7	16.5	77.7	
Savings on ART-LUM (USD) (c-d)	4,246	13,159	31,523	124,970	173,898
Age-specific percent of total saving on ART-LUM	2.4	7.6	18.1	71.9	

[a] Age-structured distribution of malaria diagnoses based on the age profile of malaria diagnoses presented in the Section 2.3

[b] Average annual number of all outpatients was extrapolated from the age-specific percent of malaria diagnoses among all outpatients in this study: < 1 year – 65.2%; 1-4 yrs - 74.5%; 5-14 yrs - 76.1% and ≥ 15 yrs – 71.7%

[c] Average annual number of performed blood slides was extrapolated from the age-specific percent of performed slides in this study: < 1 year – 39.6%; 1-4 yrs - 54.3%; 5-14 yrs – 79.3% and ≥ 15 yrs – 72.9% (Section 6.3.4.)

[d] Average annual number of positive and negative blood slides was extrapolated from the age-specific percent of routine microscopy reports in this study: < 1 year - 52.3%; 1-4 yrs - 62.7%; 5-14 yrs - 56.2% and ≥ 15 yrs - 39.6% (Section 6.3.5.)

[e] Average annual number of patients with a positive blood slide receiving an antimalarial treatment was extrapolated from the age-specific percent of routinely reported positive slides having antimalarial treatment prescribed in this study:
< 1 year - 97.1%; 1-4 yrs - 98.9%; 5-14 yrs -95.1% and ≥ 15 yrs – 95.9% (Section 6.3.6.)

[f] Average annual number of patients with a negative blood slide receiving an antimalarial treatment was extrapolated from the age-specific percent of routinely reported negative slides having antimalarial treatment prescribed in this study:
< 1 year - 66.6%; 1-4 yrs - 68.8%; 5-14 yrs -75.0% and ≥ 15 yrs – 77.7% (Section 6.3.6.)

[g] Average annual number of patients having antimalarial treatments prescribed when a blood slide was not done was extrapolated from the age-specific percent of antimalarial prescriptions for patients not having blood slide done in this study: < 1 year - 53.7%; 1-4 yrs - 58.9%; 5-14 yrs -36.8% and ≥ 15 yrs - 36.3%

[h] Cost of SP treatment was calculated on the basis of the age-specific SP dosing schedule and attributed cost per tablet cited by the MSH International Drug Price Guide: < 1 year – ½ tab (0.013 USD); 1-4 yrs – 1 tab (0.026 USD); 5 -14 yrs - 2 tabs (0.052 USD) and ≥ 15 yrs – 3 tabs (0.078 USD)

[i] Cost of ART-LUM treatment was calculated on the basis of the age-specific ART-LUM dosing schedule and attributed cost per tablet based on WHO agreement with Novartis: < 1 year – 6 tab (0.9 USD); 1-4 yrs – 12 tab (1.4 USD); 5 -14 yrs - 18 tabs (1.9 USD) and ≥ 15 yrs – 24 tabs (2.4 USD); **SP** = sulfadoxine-pyrimethamine; **ART-LUM** = artemether-lumefantrine; **BS** = blood slide; **AM** = antimalarial

However, the change of any clinical practice is a challenging task and better understanding is needed of why these practices, such as non-respect of negative malaria slide results, occur. There could be several possible explanations. First, it may be that clinicians view blood slide diagnosis as a tool to confirm their clinical suspicion of malaria rather than to rule out malaria as a contributing cause of illness, particularly when the clinical examination does not reveal another obvious illness or is highly suggestive of malaria. If this hypothesis is true then the primary focus of intervention to improve upon current practices should be the clinicians' knowledge on the role of microscopy in the management of malaria.

Second, the ambiguous text from the NMCP guideline stating that *"in certain cases a slide may be negative even when the patient has malaria"* (MoH, 1998), may have an additional effect in supporting the clinicians reasoning that malaria microscopy is only a tool to confirm their clinical suspicion but not to exclude malaria. Similar recommendations can be found in international guidelines (Section 1.5.2.2). Such recommendations convey ambiguous messages to clinicians and may undermine the real objective of introducing microscopy into peripheral facilities. A common explanation for such ambiguous recommendations is that parasites may be sequestered in the deep capillaries, and organisms may not be seen in circulating peripheral blood (Moody, 2002). However, none of the referenced documents supported this statement by any data and an extensive search of the literature could not reveal any data supporting this hypothesis relevant to the management of uncomplicated malaria. Since the critical aspect of any guideline for the successful translation of the policy into the practice is to

be explicit, the revision of the national NMCP guideline to an unambiguous statement is urgently required.

Third, clinicians may lack confidence when negative malaria slide results are reported through routine microscopy, and then doubt the quality of readings of a negative malaria slide. If a malaria slide result is truly unreliable, then clinicians' deferring to presumptive treatment for negative results seems understandable, however, the results on the accuracy of malaria microscopy discussed in the following section only partly support this hypothesis. Nevertheless, even if this hypothesis were true, it remains irrational that clinicians continue to request microscopy at all.

6.4.3 Quality of the routine malaria microscopy

Two major findings of the assessment of the quality of routine malaria microscopy were: 1) in older children and adults, clinicians should have some confidence that a blood slide reported routinely as negative is truly negative, however, they cannot be confident that laboratory reports of positive malaria slides are truly positive; and 2) the qualitative aspects of malaria microscopy such as staining of malaria smears, density quantification, species differentiation and quality control are mainly sub-optimal.

The finding that in older children and adults, the negative predictive value of routine microscopy was 91.7% overall, remaining high in low (89.4%) as well as in high (93.7%) malaria endemic areas should provide some confidence among clinicians that negative slides are truly negative. The results are in accordance with the studies performed in high

endemic areas and across all age groups from Kenya (Barat & Kramer, 1999), Zambia (Barat *et al.*, 1999) and Benin (Holtz & Kachur, 2000) where NPVs were consistently greater than 93%. However, the high NPV partly reflects the fact that in both high and low transmission settings in this study the prevalence of confirmed malaria was low in this age group. The low prevalence of 'true malaria' in both transmission settings in those aged 5 or more years (10% in the high transmission area and 17% in the low transmission area) also in part explains the low positive predictive value of routine microscopy for detecting true malaria in both settings. Thus approximately 4 of 5 routinely reported positive slides were in fact negative. These findings are similar, to those from a recent study in Tanzania where the positivity rate of research slides among patients above 5 years of age admitted to hospital with severe malaria did not differ between lowland, high (19%) and highland, low (22%) malaria transmission settings (Reyburn *et al.*, 2004). However, while the low prevalence of true malaria in this age group helps explain the low positive predictive values there is clearly a major problem with the accuracy of routine microscopy. Even at a prevalence of true malaria of 10% the positive predictive value of routine microscopy could rise to 50% if routine microscopy was 90% sensitive and 90% specific compared with gold standard microscopy – unfortunately accuracy targets well above those reported in this study.

This study suggested that a single change of diagnostic practice, respecting negative parasitological results, could produce significant savings in older children and adults under ART-LUM treatment policy in Kenya even if the accuracy of microscopy was not improved. However, this would be done at the cost of reducing sensitivity for identifying

true cases by 33% and would result in 1 of 23 outpatients above 5 years of age being sent home without an antimalarial drug when they are in fact parasitaemic. The risks of such a trade-off are essentially unknown, however, they might be expected to be low in older children and adults with uncomplicated malaria who are considerably less vulnerable to developing severe, potentially fatal complications.

Finally, it should be acknowledged that the ideal solution, reducing the risk of failure to treat true cases and creating even more significant antimalarial drug cost savings, would be improvement in the accuracy of malaria microscopy accompanied by a change of diagnostic practice. An ideal 100% accuracy of malaria microscopy is probably an unrealistic target under field conditions. Sensitivities and specificities of above 90% are not unreasonable standards for a laboratory quality assurance scheme and likely to be acceptable targets to justify interventions focusing on a change of clinical diagnostic practice.

The condition of facilities accommodating the laboratories, with only 55.9% having electricity and 50.0% having running water, is significantly below the standards set up by the national laboratory policy guideline (MoH, 1995). Given the lack of electricity in more than half of the facilities, the presence of light microscopes in 52.9% facilities and not the electric ones recommended by the guideline, is a rational decision. In this aspect the standards set up in the policy guideline should incorporate and better reflect the scarce resources of the peripheral health facilities. More than two-thirds of laboratories use rapid Field's method for routine staining of malaria smears rather than more complex

to use Giemsa staining method. Although the species differentiation was reported to be routinely performed from more than half of the laboratories, none of the evaluated patients' positive reports contained specification of *Plasmodium* species and only 23.5% of laboratories reported routinely performing malaria thin smears, an appropriate smear for species differentiation. Routine quantification of parasitaemia was reported from 76.5% of laboratories and the result conforms to 30.0% of positive patients laboratory reports without parasite densities specified. However of all patients with reported positive results only 23.3% children and 8.7% patients above 5 years of age had a reported parasitaemia greater than one plus or scanty. Given the low rate of true positive results and complete absence of quality control it appears that reports of low parasitaemia may reflect a "practice of convenience" in busy and understaffed laboratories where a clinician might "expect" a positive result.

6.4.4 Implications of the study findings on malaria diagnostic strategies in Kenya

The recent change of national antimalarial drug policy towards ART-LUM (MoH, 2004b), with a 30-fold more expensive adult treatment course compared to SP, a more complex administration schedule and less certain safety profile (WHO, 2001a), suggests the need for adequate, laboratory supported, malaria diagnostic strategies to rationalise antimalarial drug use. However, it seems evident that the major impact of microscopy, as it is performed currently, is not reduction in the use of antimalarial drugs but more unnecessary additional cost and time wasted by patients at facilities with microscopy. Therefore, rather than expanding malaria microscopy into additional facilities in Kenya, emphasis should be placed on the improvement of the effectiveness of this service at

facilities where it already exists and careful consideration of alternative malaria diagnostic strategies. In the light of the findings of this study, the following programmatic recommendations, on laboratory supported, malaria diagnostic strategy can be made:

1) Development of unambiguous clinical guidelines specifying how to use and interpret malaria slides in different age groups and areas of malaria endemicity.
2) Improvement of existing microscopic services by developing standard operating procedures, improving accuracy of malaria slide reading by further training of microscopists, and most importantly, introducing effective supervision and quality control.
3) An alternative malaria diagnostic strategy using rapid diagnostic tests should be considered and under prospective, rigorous trials its cost-effectiveness should be evaluated.

6.4.4.1 Development of clinical guidelines

Development of unambiguous clinical guidelines addressing the effective use of microscopy should take into consideration particular age groups, areas of endemicity or specific clinical situations where the major impact on the reduction of antimalarial drug use, or on patient care, can be expected. Furthermore, from a pragmatic point of view, the guidelines should also reflect the reality of health services in Kenya at different levels and their capacities to implement effectively such services.

Bearing in mind the above concerns, only febrile patients, defined as those with increased temperature or history of fever during the present illness, should be considered for malaria microscopy. Due to the large number of patients attending these facilities, it would be impossible to examine blood slides on all patients presenting with fever. Therefore, the use of microscopy should be promoted in febrile older children and adult patients, a less vulnerable age group with lower risk of severe malaria compared to children. In this patient group the largest reduction of drug costs would be made (Table 6.11).

Children below 5 years in areas of high malaria endemicity are the age group with the highest risk of dying, carrying the largest malaria burden but consuming the lowest cost of antimalarial drugs; therefore, given the limited capacities of health services and the least impact on drug use and the cost, presumptive treatment of all fevers for malaria would be a reasonable approach in most malaria settings countrywide. Furthermore, such recommendations would be in accordance with already established and promoted IMCI guidelines.

In areas of low malaria endemicity, defined conservatively by IMCI as areas where less than 5% of childhood fevers are due to malaria, the role of microscopy might be promoted in febrile children, but with the probable exception of Nairobi and Central Province few such areas exist in Kenya. In such areas IMCI currently recommends that fever in the absence of measles, running nose or any other identifiable cause of fever presents a clinical indication to treat children for malaria. It might be expected that the

use of laboratory diagnosis, may complement or replace clinical criteria to improve malaria diagnostic specificity, however, this remains to be evaluated.

Furthermore, children as well as adults, regardless of the malaria endemicity, should be evaluated for potential treatment failures and sent for microscopy if fever persists in spite of antimalarial treatment. Herein, IMCI recommendations should be complemented to address use of microscopy for such specific clinical situations, where a significant impact on patient care can be expected. With regard to the interpretation of malaria slides, the guidelines should be explicit and discourage prescription of antimalarial drugs when parasites are not seen, and in particular for patients presenting with uncomplicated malaria.

6.4.4.2 Improvement of microscopic service

It has to be acknowledged that the quality of malaria microscopy depends absolutely on good techniques, availability of reagents and microscopes, and notably, well trained and supervised technicians. Furthermore, the quality control of malaria blood slides presents one of the key components assuring the accuracy of malaria microscopy. Unfortunately, at this point in time, quality control is virtually non-existent in Kenya. This four-district study, together with the study from Bungoma district (Barat & Kramer, 1999), revealed significant deficiencies in microscopic services in Kenya with high rates of inaccurate readings. It is important that further training is urgently provided to existing microscopists. However, if adequate quality of microscopy cannot be achieved, microscopic diagnosis is an unreliable tool that uses up scarce resources for doubtful

benefits. Under such conditions, an improvement of clinical practices in accordance with guidelines would remain sub-optimal.

6.4.4.3 Malaria rapid diagnostic test as an alternative diagnostic tool

A potential solution to overcome the limitations of microscopy under field conditions is the introduction of RDTs, which are intended to allow simple and precise diagnosis of malaria in areas where standard laboratory diagnosis is not available or the quality cannot be maintained. Ideally, RDTs should offer high sensitivity, specificity, rapidity, ease of performance and interpretation, species differentiation, allow for quantitative analysis, ability to be stored under ambient conditions, and all at an affordable price. Currently, most of these performance characteristics are either achieved or in the process of refinement by the industry, yet the main obstacle for widespread use of RDTs, and in particular those detecting pLDH antigen which overcome the problem of persistent HRP-II antigaenemia, is their cost (WHO, 2000b). However, it could be expected that the increasing cost of first-line treatments will raise demand for RDTs that will force prices down and make this diagnostic tool more widely available.

Yet, the translation of any diagnostic tool into effective practice resulting in better case management still needs to be demonstrated. It is plausible that clinicians may "believe" rapid test results more than blood slides if the tests are highly sensitive, performed by themselves and introduced into the clinical practice as highly accurate tools. However, to prove these hypotheses, prospective, cost-effectiveness intervention trials under truly

operational conditions across different areas of malaria endemicity are required to provide better evidence on the true influences of RDTs on health workers practices.

CHAPTER 7:

Conclusions

7.1 Introduction

The three major areas of this thesis include: 1) evaluation of the quality of malaria case management in children (Chapter 3) and examination of factors influencing health workers treatment practices (Chapter 4); 2) description of the quality of routine clinical assessment, the accuracy of malaria diagnosis and exploration of the ability of clinical signs and symptoms to identify malaria in older children and adults (Chapter 5); and 3) description of the effects of routine microscopy on malaria case management (Chapter 6). In this Chapter the key findings presented and discussed in previous chapters are summarised, the implications of the findings for Kenyan and international contexts are highlighted, and some of the areas that demand further investigation are identified.

7.1.1 Quality of malaria case management in children

- The majority of fever episodes in sick children were detected by health workers and most fevers were diagnosed as malaria in line with national recommendations
- Performance of more complex clinical assessment tasks that are important for the detection of severe malaria and counselling of caratekers were sub-optimal
- Nearly all health facilities had SP in stock, however, only 45% of health workers had been trained on new protocols, 58% were in possession of guideline and only 27% of facilities had malaria treatment wall charts
- Among children with uncomplicated malaria, only 55% had the recommended first-line treatment prescribed and 34% of children left a health facility either without any antimalarial treatment, or with a prescribed antimalarial drug that was either ineffective or given in a dose insufficient to cure malaria effectively

The prompt detection and diagnosis of all fevers as malaria is an important step in ensuring access of febrile children to antimalarial treatment at health facilities in Kenya. Current practice is largely successful in achieving this. However, the sub-optimal performance of more complex assessment tasks indicates that current practices are likely to miss an important group of sick children with severe disease and poor prognosis. Perhaps, it was not surprising that the counseling component was the weakest part of the clinical process in the study. In the past, counseling standards have frequently been neglected in various malaria specific guidelines and only recently, with the introduction of IMCI guidelines, has its importance been emphasised. In Kenya, the adequate performance of counselling is gaining increasing significance with the change of policy towards ART-LUM treatment, a drug with more complex pharmacokinetic properties than SP and requiring a more complicated dosing schedule. Thus, patients' adherence and appropriate drug administration at home will be critical to achieving the full clinical and public health utility of ART-LUM. The quality of health workers counseling may be a major determinant of this process.

Although malaria is commonly diagnosed, sub-optimal treatment practices mean that children are not guaranteed access to effective antimalarial treatment at government health facilities in Kenya. A number of useful lessons should be considered for the future implementation of new antimalarial drug policies. Three years after the policy changed from chloroquine to SP in Kenya bottlenecks in the provision of in-service training and job aides are still common and changing clinical practice remains a significant challenge even when inexpensive and simple to administer drugs such as SP are recommended.

Deciding on a new drug policy is arguably the easier part of a complex process that should result in effective delivery of antimalarial treatment. With the announcement of a new ART-LUM treatment policy in Kenya and limited health workers' experience with this drug that is more complex to use, it is clear that considerable attention to the process of implementation will be necessary to achieve effective treatment.

7.1.2 Predictors of the quality of health worker treatment practices

- Associations between several programmatic interventions (such as in-service malaria training, distribution of guidelines and wall charts, and more frequent supervision), and the quality of health worker treatment practice for uncomplicated malaria have been demonstrated

It was encouraging to observe that the MoH's limited efforts at implementing the malaria treatment policy seemed to influence health workers' treatment performance. However, generalising these findings beyond Kenyan borders should be undertaken cautiously. Previous studies with a similar design have suggested that some of the programmatic interventions identified as improving performance in this study are only sometimes associated with improved treatment practice, and on occasions even associated with more errors. Given the discordant results between various studies, and the fact that in-service training and provision of job aids are major programmatic activities of many malaria control programmes, it is clear that an appropriate question requiring further investigation is what are the common characteristics of "successful" interventions and what are their most cost-effective combinations?

Analyses of the predictors of health worker performance using data from cross-sectional surveys are useful, yet unsatisfying. They are helpful for generating hypotheses, but the strength of the evidence is generally insufficient to support a convincing conclusion of causality. What is urgently needed are prospective, cost-effectiveness intervention trials that serve the dual purpose of providing programmatic guidance on how to strengthen and maintain health worker practices while providing better evidence on the factors that most powerfully influence health worker performance.

7.1.3 Quality of clinical assessment, accuracy of current malaria diagnosis and ability of clinical signs and symptoms to predict malaria in older children and adults

- Health workers' performance of clinical assessment tasks aimed at determination of alternative causes of fever was commonly poor
- Current diagnostic practice equates nearly all fevers with malaria and results in a massive overdiagnosis of malaria in older children and in adults, in areas of different malaria endemicity
- However, algorithms based on clinical signs and symptoms show little promise of being able to improve our ability to predict malaria in febrile older children and adults

In older children and adults, the sub-optimal performance of clinical assessment and massive overdiagnosis of malaria leads to wastage of antimalarial drugs, increased exposure to adverse drug effects, potential failure to diagnose other fever-causing conditions and a greater likelihood of emerging antimalarial drug resistance. In fact in

Kenya, the majority of malaria diagnoses are made in older children and adults, resulting in a disproportionate consumption of antimalarial drugs in a population at lower risk of morbidity and mortality. From the cost perspective, the problem of the overdiagnosis of clinical malaria will become even more important with deployment of ART-LUM that is 30-fold more expensive for a treatment course in adults than SP.

While health workers clearly overdiagnose malaria what is the possibility of using a clinical approach to improve their diagnostic accuracy? These data suggest that it is unlikely that the accuracy of malaria diagnosis can be improved based on clinical criteria alone. The findings of this study on clinical predictors of malaria thus support previous studies with similar conclusions. The use of parasite-based diagnosis is the only potential solution to improve malaria diagnostic accuracy and reduce the number of unnecessary treatments and costs. At the same time the clinical consultation and examination needs to be substantially improved to ensure adequate diagnosis of non-malaria conditions.

7.1.4 Effects of microscopy on malaria case management

- The clinicians interpretation of malaria smear results was characterised by an overwhelming tendency to ignore negative malaria smear results and continue to prescribe antimalarial drugs
- The quality of routine malaria slide reporting was poor with considerable overreporting of positive slides, however, most of the results routinely reported as negative were truly negative

In concluding that parasite-based diagnosis is a key requirement of improving the targeting of malaria treatment this clearly demands an accurate diagnostic service. The data on malaria microscopy in this study highlight major deficiencies in clinical and laboratory practices that need to be addressed if the problem of malaria overdiagnosis is to be overcome by promoting any parasite-based diagnostic strategy for widespread use in peripheral facilities in Kenya. Sub-optimal accuracy of blood slide readings in this study may be explained by the absence of any standard operating procedures, lack of quality control in operating laboratories and insufficient in-service training of microscopists. All of these programmatic activities are urgently required. At present it seems quite evident that the current, major impact of microscopy, rather than a reduction in the use of antimalarial drugs, is unnecessary additional cost and time wasted by patients at facilities where this service is available.

A potential solution to overcome the complex technical aspects of microscopy is the introduction of rapid diagnostic tests, which are simple and quick to perform, easy to interpret, can be stored under ambient conditions, and therefore have a potential to be deployed into rural health facilities where laboratories and qualified staff are not available. Yet, the ability to translate such a diagnostic tool into effective practice resulting in better case management still needs to be demonstrated. It is plausible however that clinicians may "believe" rapid test results more than blood slides if the tests are highly sensitive, performed by themselves and introduced into clinical practice as highly accurate tools. However, to prove these hypotheses, prospective, cost-effectiveness intervention trials under truly operational conditions in different areas of

malaria endemicity are required to provide better evidence on the true influence of RDTs on health workers' practices.

This study has demonstrated that a careful review of malaria diagnostic strategies is required countrywide. Regardless of the choice of the malaria diagnostic tool, of paramount importance is that policy makers ensure that the introduction of diagnostics is accompanied with clear instructions on their use and interpretation. At present Kenyan and international guidelines continue to promote the concept that a negative malaria test does not exclude malaria. The permitted option to ignore a negative test seems to undermine all other improvement approaches. As such, the development of guidelines presents only the first step in the implementation of diagnostic strategies. The provision of effective in-service training, dissemination of guidelines, translation of guidelines into simple job aids such as malaria diagnostic and treatment wall charts, and more frequent supervision of both clinical and laboratory health workers are minimal requirements necessary to ensure that a malaria diagnostic strategy is going to be successfully implemented. Although changing clinical practice remains a challenge, several retrospective and prospective studies including this one, support the view that these programmatic interventions may be successful and improve health workers clinical management in accordance with standards.

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Appendices

Appendix I

Division of Malaria Control, Ministry of Health
Malaria Case Management – Quality of Care Survey
Direct observation study
(Form DOMC/HF1)

ID Number.....[__]-[__|__|__]-[__]-[__|__|__]

Date .....[__|__] [__|__] [__|__]

Name of District.....[_____]
Name of HF.....[_____]
Interviewer initials.....[_____]
Name of Health Worker .....[_____]

Child's name .....[_____]

Consultation starting time.....[__|__]**hours** [__|__]**min**
Consultation interrupted at (in case) .....[__|__]hours [__|__]min
Consultation continued at (in case) .....[__|__]hours [__|__]min

1. General questions

a. Did the HW **greet** mother?(Y/N) .....[__]

b. Did the HW ask if this is **the first visit for this illness** to this facility? (Y/N).....[__]

c. Does HW determine child's **age?** (Y/N) .....[__]
If yes, is it done by:
Asking caretaker.....[__]
Examining child's health card.....[__]
Other (specify) .....[_____][__]

d. Does HW determine child's **weight**? (Y/N) .....[__]
If yes, is it done in a way that:
HW weighs the child that day .....[__]
Other OPD staff weighs the child that day.....[__]
HW reviews previous child's records.....[__]
Other (specify).....[_____][__]

e. Does HW determine **weight for age** in child's health card? (Y/N) .....[__]

[__]-[__|__|__]-[__]-[__|__|__]

f. **Why** did mother bring the child? (*mark only Y for complaints mentioned without prompting*)

fever ..... [__]
cough ..... [__]
difficult breathing ..... [__]
not eating well ..... [__]
vomiting ..... [__]
diarrhoea ..... [__]
malaria ..... [__]
ear problem ..... [__]
convulsions ..... [__]
stomach ache ..... [__]
skin problem ..... [__]
headache ..... [__]
other (specify) ..... [__][_____]
other (specify) ..... [__][_____]

2. Fever/temperature assessment

Did the Health worker do the following:

a. Ask if the child has **fever**? (Y/N) ..... [__]

b. Ask for **how long**? (Y/N) ..... [__]

c. Measure the temperature with **thermometer**? (Y/N) ..... [__]

d. **Feel** the child to see if the child is hot? (Y/N) ..... [__]

3. General danger signs

a. Is the child **awake** and **alert**? (Y/N) ..... [__]
If no, did the HW try to **wake** the child? (Y/N) ..... [__]

b. Does health worker ask:

If the child is able to **drink** or **breastfeed**? (Y/N) ..... [__]

If the child **vomits** everything? (Y/N) ..... [__]

If the child has had **convulsions**? (Y/N) ..... [__]

[__]-[__|__|__]-[__]-[__|__|__]

4. Clinical history

Does Health worker ask:

a. If the child has **cough** or **difficult breathing**? (Y/N) ..... [__]

b. If the child has **diarrhoea**? (Y/N) ..... [__]

c. If the child has an **ear problem**? (Y/N) ..... [__]

5. Malaria assessment

a. HW looks for **conjunctival pallor**? (Y/N) ..... [__]

b. HW looks for **palmar pallor**? (Y/N) ..... [__]

c. HW checks for **splenomegaly**? (Y/N) ..... [__]

d. HW checks for **skin pinch**? (Y/N) ..... [__]

e. HW **counts breaths**? (Y/N) ..... [__]
If Yes,
How long? *<30sec* ☐ *30-59sec* ☐ *60sec and more* ☐

f. Was the patient **positioned to view signs** of chest indrawing or deep breathing? (Y/N) ..... [__]

g. Did the HW have the child **undressed** for examination? (Y/N) ..... [__]

h. Did HW use **stethoscope**? (Y/N) ..... [__]

i. Did HW ask about previous **skin reactions** when taking SP? (Y/N) ..... [__]

j. Did the HW ask about previous use of **drugs** during the **present** illness? (Y/N) ..... [__]
If Yes, **which drugs** caretaker reported?

6. Laboratory requests

a. BS requested (Y/N) ..... [__]
b. HB requested (Y/N) ..... [__]
c. Blood sugar requested (Y/N) ..... [__]

[__]-[__|__|__]-[__]-__|__|__]

7. Diagnosis and treatment

a. Did the **HW tell** the caretaker child's **diagnosis?** (Y/N) ..... [__]

b. Write out exactly **what diagnosis the HW told** the caretaker:

c. Did the **HW tell** the mother **what treatments** to give to the child? (Y/N)..... [__]

d. Did the **HW explain how to give** the medication? (Y/N)..... [__]

e. Write out exactly **what was explained** to the caretaker:

f. Did the HW explain about **tepid sponging**? (Y/N)..... [__]
g. Did the HW advise the caretaker to give **extra fluid**? (Y/N)..... [__]

8. Caretaker counseling

a. Has a course of **antimalarials** been prescribed by the HW? (Y/N)..... [__]
If Yes, does the HW
observe the child taking **STAT dose**? (Y/N) ..... [__]
advises caretaker what to do in case of **vomiting**?(Y/N)..... [__]

b. Did the HW tell the mother to **continue feeding or breastfeeding**? (Y/N)..... [__]

c. Did the HW ask the mother to return immediately if the child is **unable to drink or breastfeed**? (Y/N)..... [__]
d. Did the HW ask the mother to return immediately if the child **becomes sicker**? (Y/N).. [__]

e. Did the HW ask the mother to return for **follow up** for this illness? (Y/N) ..... [__]
If Yes, in **how many days**? .....[__|__]
f. Were you asked to come back **if fever persists**?(Y/N) ..... [__]
If Yes, in **how many** days? .....[__|__]

g. Did the HW ask the mother if she has **any questions**? (Y/N)..... [__]
h. Was the patient **referred**? (Y/N)..... [__]
If Yes, where to ..... [_____]

Consultation ending time[__|__]hours [__|__]min

Appendix II

Division of Malaria Control, Ministry of Health
Malaria Case Management – Quality of Care Survey
Exit interview
(Form DOMC/HF2)

ID Number.....[__]-[__|__|__]-[__]-[__|__|__]

Date .....[__|__] [__|__] [__|__]

Name of District.....[_____]
Name of HF.....[_____]
Interviewer initials.....[_____]
Name of Health Worker .....[_____]

Child's name .....[_____]

Arrival time to the health facility .....[__|__]hours [__|__]mins
Departure time from the health facility .....[__|__]hours [__|__]mins

1. General questions:

a. Did the HW **refer** your child to another facility (hospital)? (Y/N).....[__]

b. Did the HW **admit** your child to this facility?(Y/N).....[__]

If yes to either a. or b. finish questionnaire with question 13 only

c. Were you **greeted** by HW? (Y/N).....[__]

d. Was the child **weighed**? (Y/N) .....[__]

e. Did you have the child's **health card** with you? (Y/N) .....[__]

f. Were you asked for child's **age**? (Y/N).....[__]

g. Did HW ask you if this is your **first visit to HF for this illness**? (Y/N).....[__]

[__]-[__|__|__]-[__]-[__|__|__]

8) Which **complaints** did you report when HW asked you? (*Mark only Y for complaints mentioned without prompting*)

fever ..... [__]
cough ..... [__]
difficult breathing ..... [__]
not eating well ..... [__]
vomiting ..... [__]
diarrhoea ..... [__]
malaria ..... [__]
ear problem ..... [__]
convulsions ..... [__]
stomach ache ..... [__]
skin problem ..... [__]
headache ..... [__]
other (specify) ..... [__][_____]
other (specify) ..... [__][_____]

9. Fever/temperature assessment

a. Did HW ask you if your child has **fever**? (Y/N) ..... [__]

b. Was fever measured by **thermometer**? (Y/N)(show thermometer) ..... [__]

c. Were you asked for **how long** child has fever? (Y/N) ..... [__]

10. General danger signs

a. Were you asked if child can **drink or breastfeed**? (Y/N) ..... [__]

b. Were you asked if child had **convulsions**? (Y/N) ..... [__]

c. Were you asked if child **vomits** everything? (Y/N) ..... [__]

11. Clinical history

a. Were you asked if child has **diarrhoea**? (Y/N) ..... [__]

b. Were you asked if child has **cough** or **difficult breathing**? (Y/N) ..... [__]

c. Were you asked if child has an **ear problem**? (Y/N) ..... [__]

[__]-[__|__|__]-[__]-[__|__|__]

12. Malaria assessment

a. Did the HW check child's **eyes**? (Y/N) ..... [__]
If Yes, Confirmed by caretaker's **demonstration**? (Y/N) ..... [__]

b. Did the HW look child's **palms**? (Y/N) ..... [__]
If Yes, Confirmed by caretaker's **demonstration**? (Y/N) ..... [__]

c. Did the HW **pinch** the child's skin?(*demonstrate*) (Y/N) ..... [__]

d. Did HW ask you about previous **skin reactions** when taking SP? (Y/N)..... [__]

e. Were you asked on previous use of **drugs** for this illness? (Y/N) ..... [__]
If Yes, **which drug** did you report? ..... [__]

f. Did you **undress** the child? (Y/N) ..... [__]

g. Did the HW use **stethoscope** to examine the child? (Y/N)(*show stethoscope*)..... [__]

h. Was the child sent to the **laboratory**? (Y/N)..... [__]
If Yes, **read from the card** and tick all laboratory results reported:

BS +ve ☐ (scanty☐ + ☐ ++ ☐ +++☐ ++++☐ other_____) **BS-ve**☐

Hb done ☐result_____ **Blood sugar** done ☐result_____other tests_____result_____

13. Diagnosis & Treatment

a. Did the HW tell you what is **wrong** with your child?(Y/N)..... [__]

If Yes, **What** did the health worker **say** was wrong with your child?

b. Which diagnosis were **written on the card**?

c. Treatment prescribed (including **name** of drug, **dose** and route of **administration**)

14. Caretaker counseling

a. Were you told to **continue feeding or breastfeeding**?(Y/N) ..... [__]

b. Were you told to give **extra fluids**? (Y/N) ..... [__]

c. Were you explained about **tepid sponging**? (Y/N) ..... [__]

d. Were you asked to return immediately if the child becomes **unable to drink or breastfeed**? (Y/N) ..... [__]

e. Were you asked to return immediately if the child **becomes sicker**? (Y/N) ..... [__]

f. Were you asked to return for **follow up** for this illness? (Y/N) ..... [__]
If Yes, in **how many days**? ..... [__|__]

g. Were you asked to come back **if fever persists**? (Y/N) ..... [__]
If Yes, in **how many days**? ..... [__|__]

h. Were you asked if you have **any questions**? (Y/N) ..... [__]

i. Were you given any **drugs** to give the child **at home**? (Y/N) ..... [__]
If yes, were you **explained** how to give the drugs at home by any of HWs? (Y/N).. [__]
If yes, **who explained it**? (Mark Y where mother specifies)
1. Clinician who saw the child ..... [__]
2. Pharmacist ..... [__]
3. Others (specify) ..... [__][_____]

h. Were you told to **buy** medication **outside** the health facility? (Y/N) ..... [__]

i. If HW explained how to give medications at home, ask caretaker to explain **how she is going to give them** (for dispensed and prescribed to buy drugs)

Name of medicine	D	P	How much each time	How many times/day	Days

j. Was the child given the **first dose of drug at the clinic**? (Y/N)..... [__]

If Yes, did any **HW observe the child swallowing** the drug(Y/N) ..... [__]

If Yes, **who observed**?

1. HW who saw the child (Y/N) ..... [__]
2. Pharmacist(Y/N)..... [__]
3. Other HW(specify) (Y/N)..... [_____][__]

k. If the child was given the first dose of drug, **which drug** was given?
(write the name(s)) ..... [_____][__|__|__]

g. Did any of HWs tell you what to do if child **vomits** medicines? (Y/N)..... [__]
If Yes, what were you **told**?

Appendix III

Division of Malaria Control, Ministry of Health
Malaria Case-Management – Quality of Care Survey
Mother/caretaker interview
(Form DOMC/HF3)

[__]-[__|__|__]-[__]-[__|__|__]

1. Child's Residence:

District ..... [_____]
Location ..... [_____]
Sub-location ..... [_____]
Enumeration Area/Village ..... [_____]
Household heads name ..... [_____]
Clan elder's/ Village Head's name ..... [_____]
Nearest school ..... [_____]
Nearest bus stage ..... [_____]
Nearest shop name ..... [_____]
Nearest HF name ..... [_____]
To be completed later:
Confirmed EA ..... [_____] – [__|__|__|__]

2. Is **the first attendance** at this facility for this illness episode(Y/N) ..... [__]

3. How much money did mother pay for:
   Laboratory examinations (KES) ..... [__|__|__|__]
   Drugs (KES) ..... [__|__|__|__]
   Consultation (KES) ..... [__|__|__|__]
   Transport (one way fare) (KES) ..... [__|__|__|__]
   Total Cost (KES) ..... [__|__|__|__]

4. Does your child's present illness involve a **fever**? (Y/N) ..... [__]

If No, end interview If Yes, Continue

5. For **how many days** has the child had a fever (Today = 1) ..... [__|__]

[__]-[__|__|__]-[__]-[__|__|__]

6. **Before** the child was brought to this HF did s/he receive **any other treatment** (Y/N) ... [__]

If yes,

*7. What was **the first** treatment (s) given to the child and its cost – unprompted (see drug chart)*

[_____] ..... [__|__][__|__|__]
[_____] ..... [__|__][__|__|__]
[_____] ..... [__|__][__|__|__]
[_____] ..... [__|__][__|__|__]

8. What was the **total cost** of treatment, tests and consultation the mother had to pay at this point of intervention (KES) ..... [__|__|__]

9. Where were these **drugs obtained from**
1.drugs kept at home; 2. shop; 3. private pharmacist; 4. private doctor; 5. community pharmacist (e.g. BI); 6. government dispensary, health centre or hospital; 7. mission dispensary, health centre or hospital; 8. other (specify_____)..... [__]

10. Provide **name** of shop or facility[_____] ..... [__]-[__|__|__|__]

11. How many anti-malarial tablets/drops or spoons given to the child in total ..... [__|__]

12. **How many days ago** was this treatment given (today = 01) ..... [__|__]

13. Were any **other treatments given after** this treatment (Y/N) ..... [__]

If yes, complete additional sheet

[__]-[__|__|__]-[__]-[__|__|__]

Caretaker - supplementary sheet

1. Is this the **1**. Second; **2**. Third; **3**. Fourth or **4**. Fifth treatment since the illness began before attending the present facility ..... [__]

2. What were the treatment (s) given to the child and its cost – unprompted (see drug chart)

[_____] ..... [__|__][__|__|__]
[_____] ..... [__|__][__|__|__]
[_____] ..... [__|__][__|__|__]
[_____] ..... [__|__][__|__|__]

3. What was the **total cost** of treatment, tests and consultation the mother had to pay at this point of intervention (KES) ..... [__|__|__]

4. Where were these drugs obtained from
1.drugs kept at home; 2. shop; 3. private pharmacist; 4. private doctor; 5. community pharmacist (e.g. BI); 6. government dispensary, health centre or hospital; 7. mission dispensary, health centre or hospital; 8. other (specify_____) ..... [__]

5. Provide name of shop or facility[_____] ..... [__]-[__|__|__|__]

6. How many anti-malarial tablets/drops or spoons given to the child in total ..... [__|__]

7. How many days ago was this treatment given (today = 01) ..... [__|__]

8. Were any other treatments given after this treatment (Y/N) ..... [__]

If yes, complete additional sheet

Appendix IV

Division of Malaria Control, Ministry of Health
Malaria Case Management – Quality of Care Survey
Service Provider Interview
(Form DOMC/HF4)

ID Number..... [__]-[__|__|__|__]-[__]
Date ..... [__|__] [__|__] [__|__]
Name of District..... [_____]
Name of HF..... [_____]
Interviewer initials..... [_____]
Name of Health Worker ..... [_____]

1. Background

a. What is the health worker's **cadre**?
Doctor..... [__]
Clinical officer..... [__]
Registered nurse ..... [__]
Registered community nurse..... [__]
Enrolled nurse..... [__]
Enrolled community nurse ..... [__]
CHW ..... [__]
Others (specify) ..... [__][_____]

b. **Age** (years)..... [__|__]

c. **Sex** (M/F) ..... [__]

d. Place of **birth** (District) ..... [_____]

e. **How long** have you worked at this facility? (years-months)..... [__|__]-[__|__]

f. Are you the facility **in-charge**?(Y/N) ..... [__]

2. Training

a. What year did you **graduate** from clinical medicine or nursing or medical school? ..... [__|__|__|__]

b. Have you ever attended an in-service training on **malaria** case management?(Y/N) ..... [__]
If No, go to question 3 **If Yes, continue**

c. Please tell us **who** was giving the course (organisation), the **year** you attended the course, the **duration** of the course, the number of **participants**, and whether the course included supervised **clinical practice**:

Who gave the course	Year	Duration (days)	No. participants	Clinical practice(Y/N)
1. _____	____	_____	_____	_____
2. _____	____	_____	_____	_____
3. _____	____	_____	_____	_____

d. Was the course based on the new **malaria guidelines** for health workers [Show example]? (Y/N)..... [__]

e. Which **in-service trainings** did you attend in the last ten years?

3. Guidelines

a. Do you **have** the new malaria guidelines for health workers [Show example]? (Y/N) .... [__]

b. Did you **read** the new malaria guidelines for health workers?(Y/N)..... [__]

c. Which **other guidelines** do you have? [List below]

4. Supervision

a. Do you have **supervision** on your job performance? (Y/N)..... [__]

If no, go to question 5 **If Yes, Continue**

b. Is the supervision done by someone **resident** (R) or someone **outside** (O) the facility? (R/O) ..... [__]

c. How many times during the last 6 months have **you met with a supervisor** about your performance? (times)..... [__|__]

d. For how many of those did he or she **observe** you take care of sick children?(times)..... [__]

e. Did you receive any **feedback** from the last supervisory session? (Y/N) ..... [__]
If yes in **which form**? (Describe)..... [_____]

Appendix V

Division of Malaria Control, Ministry of Health
Malaria Case-Management – Quality of Care Survey
Health facility assessment
(Form DOMC/HF5)

ID Number..... [__]-[__|__|__]

Date ..... [__|__] [__|__] [__|__]

Name of District..... [_____]
Name of HF..... [_____]
Interviewer initials..... [_____]

1. Observation

a. Is there a functioning **weighing scale**? (Y/N)..... [__]

b. Are all sick children **weighed**?(Y/N)..... [__]

Those that are weighed,
Where are they weighed? (Y/N)
1. At a separate **weighing station** before examined..... [__]
2. In the **consultation** room ..... [__]
3. Other (specify)..... [__] [_____]

c. Is there a functioning **thermometer**? (Y/N)..... [__]

If **Yes**, how many?(number) ..... [__|__]

d. Do all sick children have **measured temperature**?(Y/N) ..... [__]

Those that have measured temperature,
Where is the temperature measured? (Y/N)
a. At a separate **station** before examination..... [__]
b. In the **consultation room**..... [__]
c. Other (specify) ..... [__] [_____]

e. Is there an **ORT corner** where mothers can give oral hydration to their children? (Y/N)[__]

[__]-[__|__|__]

f. Are there exposed **wall charts?**(Y/N) ..... [__]

If Yes, which charts? (write the names of all charts)

g. Are **records** kept of sick child visits?(Y/N) ..... [__]

If Yes, where are they kept? (Check all that apply)

On a card given to the mother ..... [__]
In a register ..... [__]
In a file kept at the clinic ..... [__]
Other (specify) ..... [__] [_____]

2. Laboratory

a. Is there a **microscope**? (Y/N) ..... [__]

If Yes,
Is the microscope **used currently**?(Y/N) ..... [__]

If No,
Why it is not used?

b. **Objective** power of microscope ..... X[_____]

c. How are **blood films** for malaria parasitology routinely prepared (Y/N):

Thick film ..... [__]
Thin film ..... [__]
Describe **staining** methods routinely used ..... [_____]

d. Is parasite **species identification** done?(Y/N) ..... [__]

e. Are parasite **densities** done for positive cases?(Y/N) ..... [__]

f. Are sub-samples of the malaria slides sent for **quality control**? (Y/N) ..... [__]

If **Yes**,
How many **positive** slides were sent in last one year?(number)..... [__|__|__]
How many **negative** slides were sent in last one year?(number)..... [__|__|__]

g. Did you receive **results** of the quality control?(Y/N) ..... [__]

h. Is there a **Haemoglobinometer**? (Y/N) ..... [__]
If Yes,
Is the haemoglobinometer **in use currently**? (Y/N) ..... [__]
If No, why it is not used?

i. Are there any **other possibilities** to determine **Hb** at the facility? (Y/N)..... [__]
If Yes, describe..... [_____]

j. Is there a **Glucometer**?(Y/N) ..... [__]
If Yes,
Is the Glucometer **in use currently**?(Y/N)..... [__]
If Not, why is not used?

k. Are there any **other possibilities** to determine blood sugar?(Y/N) ..... [__]
If Yes, describe..... [_____]

[__]-[__|__|__]

3. Pharmacy checklist

For each of the following items check quantity **in stock** and for how long lasted **stock outs** in the last 6 months:

DRUGS	PREPARATION	QUANTITY IN STOCK NOW	STOCK OUT TIME PERIOD
Chloroquine syrup			
Chloroquine tabs			
Chloroquine inj.			
SP tablets			
SP syrup			
Amodiaquine tab			
Amodiaquine syrup			
Quinine tabs			
Quinine inj			
Other antimalarials:			
Paracetamol tabs			
Paracetamol syrup			
Other antipyretics:			
Benzyl penicilline vials			
Chloramphenicol vials			
Other injectable AB:			
Dextrose 50% vial			
Dextrose 25% vial			
Dextrose 5% bottle			
Diazepam inj			
Paraldehyde inj			
Phenobarbitone inj			
ORS sachets			
Water for inj.			

[__]-[__|__|__]

ITEM	QUANTITY IN STOCK NOW	STOCK OUT TIME PERIOD
Needles 21 G	_____	_____
Needles 23 G	_____	_____
Other needles		
_____	_____	_____
Syringe 2 ml	_____	
Syringe 5 ml	_____	_____
Syringe 10 ml	_____	_____
Spinal needles		
_____	_____	_____
_____	_____	_____
NG tubes		
_____	_____	_____
_____	_____	_____
IV giving set	_____	_____
Blood bags	_____	_____
Blood giving sets	_____	_____
Stethoscope	_____	_____
Otoscope	_____	_____
BP machine	_____	_____
Tongue depressor	_____	_____

Appendix VI

Division of Malaria Control, Ministry of Health
Malaria Case Management – Quality of Care Survey
Direct observation study

ID Number..... [__|__]-[__|__|__]

Date .....[__|__] [__|__] [__|__]

Name of HF..... [_____]

Name of Health Worker ..... [_____]

Patient's name..... [_____]

Consultation starting time.....**[__|__]hours [__|__]min**

Consultation interrupted at (in case) ..... [__|__]hours [__|__]min

Consultation continued at (in case) ..... [__|__]hours [__|__]min

1. General questions

a. Did the HW **greet** patient?(Y/N)..... [__]

b. Did the HW ask if this is **the first visit for this illness** to this facility? (Y/N)..... [__]

c. Does HW determine patient's **age**? (Y/N)..... [__]

d. Does HW determine patient's **weight**? (Y/N) ..... [__]

e. **What are the patient's main complaint(s)**? (*mark only Y for complaints mentioned without prompting*)

fever ..... [__]

chills ..... [__]

shivering ..... [__]

headache ..... [__]

joint pain ..... [__]

general body weakness ..... [__]

neck pain ..... [__]

nausea ..... [__]

cough ..... [__]

difficult breathing ..... [__]

chest pain ..... [__]

running nose ..... [__]

throat problem ..... [__]

lack of appetite ..... [__]

vomiting ..... [__]

diarrhoea ..... [__]

constipation ..... [__]

malaria ..... [__]

ear problem ..... [__]

stomach ache ..... [__]

skin problem ..... [__]

other (specify) ..... [_____][__]

other (specify) ..... [_____][__]

2. Fever/temperature assessment

Did the Health worker do the following:

a. Ask if the patient has **fever**? (Y/N) ..... [__]

b. Ask for **how long**? (Y/N) ..... [__]

c. Ask if fever is present **every day**? (Y/N) ..... [__]

d. Measure the temperature with **thermometer**? (Y/N) ..... [__]

e. **Feel** the patient to see if the patient is hot? (Y/N) ..... [__]

3. Clinical history

Does Health worker ask:

a. If the patient has **throat problem?** (Y/N) ..... [__]

b. If the patient has **running nose?** (Y/N) ..... [__]

c. If the patient has **cough?** ..... [__]

If Yes, does HW ask for **duration of cough?** (Y/N) ..... [__]

e. If the patient has **difficulties in breathing?** (Y/N) ..... [__]

f. If the patient has **chest pain**? (Y/N) ..... [__]

g. If the patient has **diarrhoea**? (Y/N) ..... [__]

If Yes, does he ask for **duration of diarrhoea?** (Y/N) ..... [__]

i. Ask if patient is **vomiting?** (Y/N) ..... [__]

j. Ask if patient has an **ear problem**? (Y/N) ..... [__]

k. Ask if patient has **chills**? (Y/N) ..... [__]

k. Ask if patient has **shivering**? (Y/N) ..... [__]

l. Ask if patient has **headache**? (Y/N) ..... [__]

m. Ask if patient has **joint pains**? (Y/N) ..... [__]

n. Record any **other** question asked by HW

[__|__][__|__|__]

4. Clinical examination

Did the Health worker do the following:

a. HW checks patient's **throat**? (Y/N) ..... [__]

b. HW checks patient's **ear**? (Y/N) ..... [__]

c. HW looks for **conjunctival pallor**? (Y/N) ..... [__]

d. HW looks for **palmar pallor**? (Y/N) ..... [__]

e. HW checks **pulse rate**? (Y/N) ..... [__]

f. HW checks **lymph nodes**? (Y/N) ..... [__]
If Yes, which nodes?

g. HW checks for **splenomegaly**? (Y/N) ..... [__]

h. HW **counts breaths**? (Y/N) ..... [__]

i. Did HW **auscultate** chest? (Y/N) ..... [__]

j. Did HW ask about previous **skin reactions** when taking SP? (Y/N) ..... [__]

k. Did the HW ask about **previous use of drugs** during the **present** illness? (Y/N) ..... [__]
If Yes, **which drugs** patient reported?

l. Record any **other clinical examination** done by HW

m. Was patient sent to **laboratory** (Y/N) ..... [__]

Consultation ending time[__|__]hours [__|__]min

Appendix VII

Temporary Patients Card

ID Number..... [__|__]-[__|__|__]

Appendix VIII

Division of Malaria Control, Ministry of Health
Malaria Case Management – Quality of Care Survey
Exit Examination Form

ID Number..... [__|__]-[__|__|__]
Date ..... [__|__] [__|__] [__|__]
Name of **HF** ..... [_____]

1. General questions

a. Patient's **name**..... [_____]

b. Patient's **age** (years) ..... [__|__]

c. **Initial or Follow up** visit for the same illness to this facility (I/F) ..... [__]

d. **What are the patient's main complaint(s)**? (*mark only Y for complaints mentioned without prompting*)

fever..... [__]
chills ..... [__]
shivering ..... [__]
headache ..... [__]
joint pain..... [__]
general body weakness..... [__]
neck pain..... [__]
nausea ..... [__]
cough ..... [__]
difficult breathing..... [__]
chest pain..... [__]
running nose..... [__]
throat problem..... [__]
lack of appetite..... [__]
vomiting..... [__]
diarrhoea..... [__]
constipation..... [__]
malaria ..... [__]
ear problem ..... [__]
stomach ache..... [__]
skin problem ..... [__]
other (specify) ..... [_____][__]
other (specify) ..... [_____][__]

2. History and Symptoms [__|__]-[__|__|__]

a. **Fever** in last 48 hrs (Y/N) ..... [____] If Yes, how many days .[____]

b. Gen body **weakness** (Y/N) ... [____] If Yes, how many days .[____]

c. Lack of **appetite** (Y/N)..... [____] If Yes, how many days .[____]

d. **Headache** (Y/N)..... [____] If Yes, how many days .[____]

e. **Joint** pains (Y/N)..... [____] If Yes, how many days .[____]

f. **Vomiting** (Y/N) ..... [____] If Yes, how many days .[____] times/day.[____]

g. **Diarrhoea** (Y/N) ..... [____] If Yes, how many days .[____] type_____

h. **Constipation** (Y/N) ..... [____] If Yes, how many days .[____]

i. **Chills** (Y/N) ..... [____] If Yes, how many days .[____]

j. **Shivering** (Y/N) ..... [____] If Yes, how many days .[____]

k. **Abdominal** ache(Y/N) ..... [____] If Yes, how many days .[____]

l. **Nausea**(Y/N) ..... [____] If Yes, how many days .[____]

m. **Cough** (Y/N) ..... [____] If Yes, how many days .[____]

n. **Difficult breathing** (Y/N) .... [____] If Yes, how many days .[____]

o. **Chest pain** (Y/N) ..... [____] If Yes, how many days .[____]

p. **Throat pain** (Y/N) ..... [____] If Yes, how many days .[____]

q. **Running nose** (Y/N) ..... [____] If Yes, how many days .[____]

r. **Other** symptoms (specify):

s. Has patient ever had **skin reaction** on previous use of **SP**?(Y/N)..... [__]

t. **Previous use of drugs** for the same illness? (Y/N)..... [__]
If Yes, which drugs (specify):

3. Clinical Signs [__|__]-[__|__|__]

a. **Temp (°C)**..... [_____] b.**Weight (kg)** ... [_____] c. **Anaemia(Y/N)** ..... [_____]

d.**Throat**_____ e. **Ear**_____

f. **RR**..... [_____] g. **Pulse**..... [_____] h.**Chest Indrawing(Y/N)**[_____]

i. **Lungs**_____

j. **Spleen (cm)** ..... [_____] k. **Liver (cm)** ..... [_____]

l. **Lymph nodes enlarged(Y/N)** [____] If Yes, which[_____]

m. **Other signs** on physical examination (specify):

4. Laboratory Results:

5. Diagnosi(e)s

a. If diagnosis is malaria, is it
treatment failure(Y/N) ..... [__]
simple (Y/N)..... [__]
severe (Y/N)..... [__]
if severe specify why_____

a. **Malaria diagnosis** according to **guidelines** (fever in the absence of other cause of fever)? (Y/N) ..... [__]

6.Treatment

a. Is patient **referred**?(Y/N) ..... [__]

b. Is patient **admitted**? (Y/N) ..... [__]

Appendix IX

Division of Malaria Control, Ministry of Health
Malaria Case Management – Quality of Care Survey
Service Provider Interview

ID Number.....[__|__]

Date .....[__|__] [__|__] [__|__]

Name of HF.....[_____]

1. Background

a. What is the health worker's **cadre**?

Doctor..... [__]
Clinical officer..... [__]
Registered nurse ..... [__]
Registered community nurse..... [__]
Enrolled nurse..... [__]
Enrolled community nurse ..... [__]
CHW ..... [__]
Others (specify) ..... [_____][__]

b. **Age** (years).....[__|__]

c. **Sex** (M/F) ..... [__]

d. **How long** have you worked at this facility? (years-months)..... [__|__]-[__|__]

e. Are you the facility **in-charge**?(Y/N)..... [__]

2. Training

a. What year did you **graduate** from clinical medicine or nursing or medical school? ..... [__|__|__|__]

b. Have you ever attended an in-service training on **malaria** case management?(Y/N) ..... [__]

If No, go to question 3 **If Yes, continue**

c. Which **year** did you attend the in-service **training** on malaria case mangement?[__|__|__|__]

d. Has the course/training included **supervised clinical practice**?(Y/N)..... [__]
e. **How many days** did the course last? .....[__|__]
d. Was the course based on the **malaria guidelines** for health workers

[Show example]? (Y/N)..... [__]

3. Guidelines

a. Do you **have** the new malaria guidelines for health workers [Show example]? (Y/N) .... [__]

b. Which **other guidelines** do you have? [List below]

c. Which **in-service trainings** did you attend in the last ten years?

4. Supervision

a. Do you have **supervision** on your job performance? (Y/N)..... [__]

If Yes, **how many** times you had supervision in the **last 6 months**? (Y/N) .....[__|__]

5. Barriers

a. What are the most difficult **problems** that you face in performing out-patient malaria case management?

b. According to your clinical experience, **which drugs satisfactorily treat malaria**? (*mark Y for all mentioned without prompting and then offer not mentioned reasons)*

1. Chloroquine (Y/N)..... [__]
2. SP (Y/N) ..... [__]
3. Amodiaquine (Y/N)..... [__]
4. Quinine (Y/N) ..... [__]
5. Other (specify) (Y/N) ..... [_____] [__]
6. Other (specify) (Y/N) ..... [_____] [__]
7. Other (specify) (Y/N) ..... [_____] [__]

Appendix X

Consent Information Sheet

Malaria outpatient case management in government health facilities in Kenya: An evaluation of current practices

- It is important that MoH provides good quality of care to patients with malaria and assessing how patients are treated in different areas helps this process.
- We are doing the study to monitor treatment of patients who may have malaria in this District
- During the study we observe how health workers treat patients and we also re-examine them to see if there are better ways to assess patients
- If you agree/ you allow your child to take part in this study an observer will be present when you are seen by a health worker and you/your child will be re-examined carefully by a study doctor, who will alter treatment if necessary, and a finger prick blood film will be prepared for microscopy if malaria is suspected . This will be done at the same time as any blood test ordered by the health worker.
- The results of malaria slides will not be available today so you/your child will not individually benefit from this test but the hope is that these results will help to improve the quality of malaria related care in the District and Kenya in the future

We now want to ask you if you would like / you will allow your child to be involved in this study

Remember:

- If you are not happy to participate in the study you/your child will still get looked after in the same way as every patient here.
- If you agree to start but then change your mind you/your child can withdraw from the study at any time and you/your child will still get looked after in the same way as every patient here.

Do you want to ask any questions?

The organizations involved in the study include:
DOMC, MoH, KEMRI, WELLCOME TRUST RESEARCH LABORATORIES

Appendix XI

Consent Agreement Sheet

I, _____ (parent / guardian of child named_____) have been informed about the study entitled:

Malaria outpatient case management in government health facilities in Kenya: An evaluation of current practices

The nature, implications, duration, purpose, voluntary nature and inconveniences that may reasonably be expected have been explained to me by:

_____*(name of person taking consent).*

I have been given the opportunity to ask questions concerning the study and these have been answered to my satisfaction.

I understand that I may at any time during the study revoke my consent without any loss or penalty

NDIO **I am happy to join/ for my child to join this study.**

Patients/Parents signature_____Date_____

Patients/Parents name _____

Village address _____

Identity card no _____